KISQALI® (ribociclib) + fulvestrant: OS benefit demonstrated vs placebo: HR=0.724 [95% CI: 0.568-0.924], \( P=0.00455 \). QOL benefit demonstrated vs placebo: HR=0.795; PFS benefit demonstrated vs placebo: HR=0.593, \( P<0.0001 \).

KISQALI + NSAI/tamoxifen + goserelin: OS benefit demonstrated vs placebo (ITT: HR=0.712 [95% CI: 0.535-0.948], \( P=0.00973 \); NSAI: HR=0.699 [95% CI: 0.501-0.976]; tamoxifen: HR=0.791 [95% CI: 0.454-1.377]). QOL benefit demonstrated vs placebo (NSAI): HR=0.759; PFS benefit demonstrated vs placebo (NSAI): HR=0.569.

**KISQALI is not indicated for concomitant use with tamoxifen.**

In both trials, OS and QOL were secondary end points; PFS was the primary end point.

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**Indications**

KISQALI is a kinase inhibitor indicated in combination with:

- an aromatase inhibitor for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, as initial endocrine-based therapy; or
- fulvestrant for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, 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.

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”), 1.1% of KISQALI-treated patients had ILD/pneumonitis of any grade, 0.3% had grade 3 or 4, and 0.1% had a fatal outcome. Additional cases of ILD/pneumonitis have been observed in the postmarketing setting, with fatalities reported.

CDK=cyclin-dependent kinase; HR=hazard ratio; ITT=intent to treat; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival; PFS=progression-free survival; QOL=quality of life.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.
When considering the best option for your patients, what is your treatment goal?

The majority of oncologists and women surveyed reported that **OVERALL SURVIVAL** is their #1 treatment goal.1,2

CDK4/6 inhibitors have changed the treatment paradigm for women with HR+/HER2- mBC.3

But not all CDK4/6 inhibitors are the same.

What if you could help make a difference in the survival of your patients with mBC?

KISQALI

MORE LIFE

SUPERIOR OVERALL SURVIVAL RESULTS IN A BROAD RANGE OF WOMEN4-6

<table>
<thead>
<tr>
<th>First treatment for advanced disease</th>
<th>First CDK4/6i after progression on ET for advanced disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>De novo patients</td>
<td></td>
</tr>
<tr>
<td>Late adjuvant relapse (DFI &gt;12 months)</td>
<td></td>
</tr>
<tr>
<td>Early adjuvant relapse (DFI ≤12 months)</td>
<td></td>
</tr>
</tbody>
</table>

KISQALI + fulvestrant—postmenopausal women

- OS benefit demonstrated vs placebo: HR=0.724 (95% CI: 0.568-0.924); P=0.00455. QOL benefit demonstrated vs placebo: HR=0.795 (95% CI: 0.602-1.050); PFS benefit demonstrated vs placebo: HR=0.593 (95% CI: 0.480-0.732); P=0.0001
- Randomized 2:1 to receive either KISQALI® (ribociclib) (600 mg) or placebo orally once daily (3 weeks on, 1 week off) + fulvestrant 500 mg, administered intramuscularly on Days 1, 15, and 29, and once monthly thereafter
- Included first-line (de novo or progression >12 months after completion of [neo]adjuvant ET) patients, early adjuvant relapsers (progression ≤12 months after completion of or during [neo]adjuvant ET), and second-line (progression following ET in the metastatic setting) patients

KISQALI + an NSAI/tamoxifen + goserelin—premenopausal (N=672)4-6

- OS benefit demonstrated vs placebo (ITT: HR=0.712 [95% CI: 0.535-0.948]; P=0.00973; NSAI: HR=0.699 [95% CI: 0.501-0.976]; tamoxifen: HR=0.791 [95% CI: 0.454-1.377]). QOL benefit demonstrated vs placebo (NSAI): HR=0.759 (95% CI: 0.561-1.028); PFS benefit demonstrated vs placebo (NSAI): HR=0.569 (95% CI: 0.436-0.743)
- Randomized 1:1 to receive either KISQALI (600 mg) or placebo orally once daily (3 weeks on, 1 week off) + NSAI (letrozole 2.5 mg or anastrozole 1 mg) or tamoxifen 20 mg orally once daily (continuous) + goserelin 3.6 mg administered subcutaneously once every 28 days
- Patients had no prior ET for metastatic disease
- KISQALI is not indicated for concomitant use with tamoxifen7

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.

Please see additional Important Safety Information throughout and [click here](#) for full Prescribing Information.
Consistently superior overall survival

Overall survival significantly improved in postmenopausal women

- **P=0.00455**
  - 28% REDUCTION IN RISK OF DEATH
  - (HR=0.724 [95% CI: 0.568-0.924])

**OVERALL SURVIVAL (ITT)**

<table>
<thead>
<tr>
<th>Event-free probability (%)</th>
<th>No. of events</th>
</tr>
</thead>
<tbody>
<tr>
<td>KISQALI arm: 187, Placebo arm: 108</td>
<td></td>
</tr>
</tbody>
</table>

42-month estimated survival rates

KISQALI + fulvestrant (95% CI: 52.0-63.2) 57.8%
Placebo + fulvestrant (95% CI: 36.9-54.5) 45.9%

- mOS not reached
- mOS not reached

mOS=median overall survival; NR=not reached.

- Results reported at 42 months were not prespecified and are observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error

**PFS results (primary end point)**

- **FIRST LINE** | 33.6 months mPFS
  - with KISQALI® (ribociclib) + fulvestrant vs
  - 19.2 months in the placebo arm (HR=0.546 [95% CI: 0.415-0.718])

**ITT** | 20.5 months mPFS (primary analysis)

- (95% CI: 18.5-23.5) with KISQALI + fulvestrant vs
- 12.8 months (95% CI: 10.9-16.3) in the placebo arm (HR=0.593 [95% CI: 0.480-0.732]; P<0.0001)

**IMPORTANT SAFETY INFORMATION (continued)**

**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, 14 of 1054 patients (1%) had >500 ms postbaseline QTcF value, and 59 of 1054 (6%) had a >60 ms increase from baseline in QTcF intervals.

mPFS=median progression-free survival.

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

Overall survival significantly improved in premenopausal women

- **P=0.00973**
  - 29% REDUCTION IN RISK OF DEATH
  - (HR=0.712 [95% CI: 0.535-0.948])

**OVERALL SURVIVAL (ITT)**

<table>
<thead>
<tr>
<th>Event-free probability (%)</th>
<th>No. of events</th>
</tr>
</thead>
<tbody>
<tr>
<td>KISQALI arm: 83, Placebo arm: 109</td>
<td></td>
</tr>
</tbody>
</table>

42-month estimated survival rates

KISQALI + ET + goserelin (95% CI: 63.5-76.0) 70.2%
Placebo + ET + goserelin (95% CI: 32.0-58.9) 46.0%

- mOS not reached
- mOS not reached

mOS=median overall survival; NR=not reached.

- Results reported at 42 months were not prespecified and are observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error

**PFS results (primary end point)**

- **NSAI** | 27.5 months mPFS
  - (95% CI: 19.1-NR) mPFS in the KISQALI arm vs 13.8 months (95% CI: 12.6-17.4) in the placebo arm (HR=0.569 [95% CI: 0.436-0.743])
  - Efficacy results based on a prespecified subgroup analysis of 495 patients who had received KISQALI or placebo with an NSAI + goserelin and were not powered to show statistical significance

**IMPORTANT SAFETY INFORMATION (continued)**

**QT interval prolongation (continued).** These 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.
**Overall survival significantly improved in postmenopausal women**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>OS (months)</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KISQALI + fulvestrant</td>
<td>40.0 (36.9-54.5)</td>
<td>0.724 (0.568-0.924)</td>
<td>0.00455</td>
</tr>
<tr>
<td>Placebo + fulvestrant</td>
<td>32.5 (28.7-39.1)</td>
<td>1.000 (0.791-1.377)</td>
<td></td>
</tr>
</tbody>
</table>

**RESULTS**

- Results reported at 42 months were not prespecified and are observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.

**FINISHLINE**

- 29.5 months mPFS (primary endpoint)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>mPFS (months)</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KISQALI + fulvestrant</td>
<td>40.0 (37.2-42.9)</td>
<td>0.546</td>
<td>0.00973</td>
</tr>
<tr>
<td>Placebo + fulvestrant</td>
<td>21.0 (18.9-22.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SAFETY INFORMATION**

- 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 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 case of sudden death was reported in MONALEESA-7 or MONALEESA-3.

- No cases of sudden death were reported in MONALEESA-7.

**OVERALL SURVIVAL (ITT)**

- Hazard ratio is based on unstratified Cox model.

- Results reported at 42 months were not prespecified and are observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.

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Median time to chemotherapy consistently not reached

Time to chemotherapy in menopausal women

30% REDUCTION IN RISK OF PROGRESSING TO CHEMOTHERAPY
(HR=0.696 [95% CI: 0.551-0.879])

TIME TO CHEMOTHERAPY (ITT)

mTTC not reached
KISQALI + ET + goserelin
(n=335)
mTTC 36.9 months
Placebo + ET + goserelin
(n=337)

• 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
• There was no prespecified statistical procedure controlling for type 1 error

IMPORTANT SAFETY INFORMATION (continued)
QT interval prolongation (continued). Assess ECG prior to initiation of treatment. Initiate treatment with KISQALI® (ribociclib) 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.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.
Quality of life consistently preserved

The EORTC QLQ-C30—a validated tool used worldwide to assess quality of life in cancer patients

The EORTC QLQ-C30 questionnaire was used to assess the quality of life (QOL) patient-reported outcomes (PRO) end point, which was defined as the time to deterioration of the global health status/QOL scale score of the EORTC by ≥10%

Pain scores were assessed using the EORTC QLQ-C30 scale (TTD ≥10%), and clinically meaningful reductions in pain were defined as >5-point change from baseline

### EORTC QLQ-C30 MEASURES

<table>
<thead>
<tr>
<th>5 functional scales</th>
<th>3 symptom scales</th>
<th>6 single items</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Physical</td>
<td>- Fatigue</td>
<td>- Dyspnea</td>
</tr>
<tr>
<td>- Role</td>
<td>- Nausea and vomiting</td>
<td>- Insomnia</td>
</tr>
<tr>
<td>- Emotional</td>
<td>- Pain</td>
<td>- Appetite loss</td>
</tr>
<tr>
<td>- Cognitive</td>
<td></td>
<td>- Constipation</td>
</tr>
<tr>
<td>- Social</td>
<td></td>
<td>- Diarrhea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Financial difficulties</td>
</tr>
</tbody>
</table>

- There was no significant difference between the arms in median TTD of global health status/QOL by ≥10%. Overall QOL worsened in both arms at end of trial

- Clinically meaningful reductions in pain were observed at cycles 11 and 22 in the KISQALI arm vs cycles 3-25 in the placebo arm. General reductions in pain were observed in both arms throughout treatment — KISQALI is not indicated for pain reduction

- These results are from the primary analysis conducted after observing 361 local PFS events

**IMPORTANT SAFETY INFORMATION (continued)**

**QT interval prolongation (continued).** Avoid the use of KISQALI® (ribociclib) 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

**IMPORTANT SAFETY INFORMATION (continued)**

**QT interval prolongation (continued).** 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® (ribociclib) 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 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 clinical trials in patients with advanced or metastatic breast cancer, increases in transaminases were observed. Across all trials, grade 3 or 4 increases in alanine aminotransferase (ALT) (10% vs 2%) and aspartate aminotransferase (AST) (7% 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 85 days and median time to resolution to grade ≤2 was 22 days for the KISQALI treatment groups.

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 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 trials, neutropenia was the most frequently reported adverse reaction (AR) (74%), and a grade 3/4 decrease in neutrophil count (based on laboratory findings) was reported in 58% 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 12 days in the KISQALI treatment groups. Febrile neutropenia was reported in 1% of patients in the KISQALI treatment groups. Treatment discontinuation due to neutropenia was 0.8%.

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.

Embryofetal toxicity. Based on findings from animal studies and the mechanism of action, KISQALI can cause fatal harm when administered to a pregnant woman. In animal reproduction studies, administration of KISQALI to pregnant rats and rabbits during organogenesis caused embryofetal 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. Across clinical trials of patients with advanced or metastatic breast cancer, the most common ARs reported in the KISQALI treatment groups (pooled incidence ≥20%) were neutropenia (74% vs 5%), nausea (45% vs 27%), infections (41% vs 30%), fatigue (33% vs 22%), leukopenia (30% vs 3%), vomiting (27% vs 16%), alopecia (24% vs 12%), headache (24% vs 22%), constipation (24% vs 16%), rash (21% vs 9%), and cough (21% vs 16%). The most common grade 3/4 ARs (reported at a pooled frequency >5%) were neutropenia (59% vs 1%), leukopenia (16% vs 3%), abnormal LFTs (9% vs 2%), and lymphopenia (5% vs 1%).

Laboratory abnormalities. Across clinical trials of patients with advanced or metastatic breast cancer, the most common laboratory abnormalities reported in the KISQALI-containing arm vs placebo arm (all grades, pooled incidence ≥20% and ≥5% higher than placebo arm) were leukocyte count decrease (94% vs 30%), neutrophil count decrease (90% vs 25%), hemoglobin decrease (66% vs 38%), lymphocyte count decrease (61% vs 26%), AST increase (47% vs 38%), ALT increase (44% vs 36%), creatinine increase (36% vs 13%), and platelet count decrease (31% vs 9%). The most common grade 3/4 laboratory abnormalities (incidence ≥5%) were neutrophil count decrease (59% vs 2%), leukocyte count decrease (32% vs 1%), lymphocyte count decrease (15% vs 4%), ALT increase (10% vs 2%), and AST increase (7% vs 2%).

The only CDK4/6 inhibitor with consistently superior overall survival and quality of life preserved, proven in 2 phase III trials

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**IMPORTANT SAFETY INFORMATION**

**Warnings and precautions.** Warnings and precautions with KISQALI include interstitial lung disease/pneumonitis, QT interval prolongation, increased QT interval prolongation with concomitant use of tamoxifen, hepatobiliary toxicity, neutropenia, and embryofetal toxicity.

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