## Transcript Details

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Navigating Treatment Goals With a CDK4/6 Inhibitor in HR+/HER2- Metastatic Breast Cancer: Addressing Barriers

**Announcer:**

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This medical industry feature, titled "Navigating Treatment Goals With a CDK4/6 Inhibitor in HR+/HER2- Metastatic Breast Cancer: Addressing Barriers," is sponsored by Novartis Pharmaceuticals Corporation. This program is intended for US health care professionals.

The speakers have been compensated by Novartis Pharmaceuticals Corporation to conduct this presentation.

And now here's your host, Dr Charles Turck.

**Dr Turck:**

In the treatment of HR+/HER2- metastatic breast cancer, how can we as health care providers strive to ensure a positive treatment experience for our patients? In the final podcast of this series, we're going to gain insights in how we can do just that.

This is ReachMD, and I'm Dr Charles Turck. Here with me today to discuss barriers to care with ribociclib, brand name KISQALI, and how she's addressed these barriers in her practice is Dr Naomi Dempsey. For those of you tuning in, KISQALI is a CDK4/6 inhibitor indicated for the treatment of adults with HR+/HER2- metastatic breast cancer. It's approved for use 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.

Now let's dive in. Dr Dempsey, welcome back.

**Dr Dempsey:**

Glad to be here.

**Dr Turck:**

We know that health care providers may face challenges when starting patients on a new treatment, including monitoring considerations, dose adjustments, meeting patients' goals, and financial barriers. Today we're going to uncover how a breast cancer specialist manages these challenges if they occur. Dr Dempsey, let's start with addressing coverage for patients. How can we address financial barriers to access when starting treatment with KISQALI?

**Dr Dempsey:**

Thank you for this question. Access to medicine is one of the more difficult aspects of ensuring the best care for our patients. Fortunately, 9 out of 10 patients have favorable coverage for KISQALI for all approved indications. There are also multiple financial assistance options available for eligible patients, and I encourage my colleagues to take advantage of this support.

**Dr Turck:**

That's good information to know. Moving on to other barriers, can you give us some insight into a patient's journey, starting with the necessary standard assessments when initiating KISQALI?

**Dr Dempsey:**

Of course. As I'm sure we can all agree, starting patients on their treatment as soon as possible is important, and fortunately, with KISQALI, there are only a few baseline assessments needed. And I let my patients know that the majority of scheduled monitoring is complete within the first 2 cycles of treatment. The assessments needed are: a complete blood count; liver function tests; measurement of electrolytes, including magnesium, phosphorus, potassium, and calcium; and electrocardiograms, or ECGs. ECGs enable health care providers to identify and address QT prolongation that may occur with KISQALI. Three ECGs are required, and they all occur within the first 30 days of treatment, making this step straightforward for both health care providers and patients.

**Dr Turck:**

With that being said, can you tell us a bit more about ECG monitoring, such as any perceptions that exist around this assessment and what one can expect in practice?

**Dr Dempsey:**
There is a perception that QT prolongation is common with KISQALI. The fact is, although KISQALI has been shown to prolong the QT interval in a concentration-dependent manner, the incidence was actually low.

When using KISQALI we monitor the QTcF, which is a special correction of the QT interval and is reported on all standard ECGs. In a pooled analysis across 3 phase III trials of 1054 pre- and postmenopausal patients treated with KISQALI plus an aromatase inhibitor or fulvestrant, 1.4%, or 15 out of 1054 patients, had a postbaseline QTcF value greater than 500 milliseconds. Additionally, 6% experienced an increase in QTcF interval greater than 60 milliseconds from baseline.

In all 3 trials, there were no reported cases of torsade de pointes, and KISQALI has been shown to prolong the QT interval in a concentration-dependent manner. Of course, it's important to remember to initiate KISQALI only in patients with a baseline QTcF of less than 450 milliseconds, and that **KISQALI is not indicated for concomitant use with tamoxifen.**

Now, understandably, not every physician's office will have capabilities for monitoring; however, Novartis Oncology Specialists may be able to provide a solution for fast, easy, and accurate ECG assessments for eligible offices. So, with this information in mind, it's important to recognize that the potential for QT prolongation is low. Also, there are resources available that allow us to treat a QT prolongation event in a straightforward manner, which gives me confidence in my treatment plan.

**Dr Turck:**

Thank you for addressing that, Dr Dempsey. For those just tuning in, you're listening to ReachMD. I'm Dr Charles Turck, and today I'm speaking with Dr Naomi Dempsey about KISQALI, a metastatic breast cancer treatment option and how we can better address barriers to care.

Back to our topic Dr Dempsey. What else should physicians know that will help them feel confident in managing adverse reactions with KISQALI?

**Dr Dempsey:**

So, what we've seen from clinical trials with KISQALI is that dose modification is an effective strategy for adverse reaction management. These dose modifications can be made stepwise by reducing the number of tablets taken. For me, having 1 tablet strength means dose reductions are simple to implement and it makes it easier for patients and their health care providers to manage adverse reactions together. This translates to no new prescriptions or additional costs to patients mid-cycle. In fact, in MONALEESA-2, managing adverse reactions with dose reductions helped some patients stay on therapy an average of 6.5 months longer than those without dose reductions. This is important and stands out to me since adherence is critical to treatment success.

**Dr Turck:**

I'm glad you brought that up. With overall survival being the number 1 treatment goal for patients with metastatic breast cancer, what are some considerations to keep in mind with KISQALI around overall survival and dose modifications?

**Dr Dempsey:**

What's impressive about KISQALI is that across all 3 randomized, double-blind, placebo-controlled phase III clinical trials, overall survival was maintained regardless of dose adjustments. So, clinicians and patients do not need to worry about giving up any efficacy of the treatment when dose reduction is required. This was based on a post hoc analysis in which the efficacy and the placebo comparator arms was not assessed.

**Dr Turck:**

Thank you for sharing that helpful insight. Could you please expand on the overall survival across those 3 phase III clinical trials?

**Dr Dempsey:**

Certainly. Specifically, in the MONALEESA-2 trial—which studied KISQALI plus letrozole versus placebo plus letrozole in 668 postmenopausal patients who received no prior therapy for advanced disease—at a median follow-up of 80 months, median overall survival was 63.9 months with KISQALI plus letrozole versus 51.4 months with letrozole alone. The hazard ratio was 0.765, with a 95% confidence interval of 0.628 to 0.932. 62.6% of patients in the KISQALI arm had at least 1 dose reduction, and the median overall survival for them was 66 months versus 60.6 months for patients without dose reductions. The hazard ratio was 0.87, with a 95% confidence interval of 0.65 to 1.18.

MONALEESA-7 studied KISQALI plus endocrine therapy with either a nonsteroidal aromatase inhibitor (or NSAI) or tamoxifen and goserelin versus placebo plus endocrine therapy and goserelin in the intent-to-treat population of 672 premenopausal patients. **KISQALI is not indicated for concomitant use with tamoxifen.** At a median follow-up of 35 months, statistical significance was established for overall survival in the intent-to-treat population. Median overall survival was not reached with KISQALI plus an NSAI and goserelin versus 40.7 months with an NSAI and goserelin alone. The hazard ratio was 0.699, with a 95% confidence interval of 0.501 to 0.976. 40.7% of patients in the KISQALI arm had 1 or more dose reductions. The median overall survival was not reached for both these patients as well as those without dose reductions. The hazard ratio was 0.79, with a 95% confidence interval of 0.46 to 1.36.

Lastly, MONALEESA-3 studied KISQALI in combination with fulvestrant versus placebo with fulvestrant in 726 postmenopausal patients. At a median follow-up of 39 months, statistical significance was established for overall survival in the intent-to-treat population. Median overall survival was not reached with KISQALI plus fulvestrant versus 40 months with fulvestrant alone. The hazard ratio was 0.724, with a 95% confidence interval of 0.568 to 0.924. 40.7% of patients in the KISQALI arm had 1 or more dose reductions. The median overall survival was not reached for both these patients as well as those without dose reductions. The hazard ratio was 0.88, with a 95% confidence interval between 0.64 to 1.21.

In all 3 of these clinical trials, overall survival was a secondary end point and progression-free survival was the primary.

**Dr Turck:**

This is all really impactful and important information, so thank you, Dr Dempsey, for sharing your perspectives on KISQALI and how health care providers can tackle potential barriers to care. It was great speaking with you today.

**Dr Dempsey:**

Thank you for having me.

**Dr Turck:**

For ReachMD, I'm Dr Charles Turck. Now, before we close, let's review some important safety information.

**Announcer:**

**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.**

Please see full Prescribing Information on this site or on **www.kisqali-hcp.com**.

**Announcer:**

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