

Novartis Kisqali® shows overall survival benefit in HR+/HER2- advanced breast cancer with consistent findings in patients with more aggressive disease

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- New MONALEESA-7 (M7) and MONALEESA-3 (M3) subgroup analysis to be presented during ASCO20 Virtual Scientific Program
- Subgroup analysis shows Kisqali plus endocrine therapy extended life compared to endocrine therapy for patients with liver metastases - showing ~47% and 37% reduction in the risk of death in M7 and M3, respectively[1]
- Visceral metastases, especially liver or brain metastases, generally signify a poor prognosis and more aggressive disease for patients[2],[3]
- Results add to body of evidence, reinforce Kisqali consistent overall survival benefit regardless of type of metastases, endocrine partner or menopausal status

EAST HANOVER, N.J., May 27, 2020 /PRNewswire/ -- Novartis today announced a new exploratory subgroup analysis of the Phase III MONALEESA-3 and MONALEESA-7 trials, to be presented during the ASCO20 Virtual Scientific Program, reinforcing the overall survival (OS) benefit of Kisqali® (ribociclib). In this subgroup analysis, Kisqali plus endocrine therapy increased OS compared to endocrine therapy alone among women with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer with visceral metastases, consistent with the benefit seen in the overall study populations.

"The analysis, looking across two Phase III trials, supports the use of Kisqali in the first-line setting regardless of menopausal status or metastatic location," said Denise Yardley, MD, Principal Investigator, Sarah Cannon Research Institute. "Patients with visceral metastases generally face worse prognosis and a higher risk for treatment resistance, so the consistent overall survival results with Kisqali combination therapy for these patients is compelling."

In the MONALEESA trials, where Kisqali was studied in premenopausal women in combination with NSAI plus goserelin (MONALEESA-7) and in postmenopausal women in combination with fulvestrant (MONALEESA-3), approximately 60% of the participants had visceral metastases (excluding visceral crisis), reflective of real-world clinical practice. In these patients, Kisqali in combination with endocrine therapy showed a 30% reduction in the risk of death in MONALEESA-7 [median OS of not evaluable (NE) vs. 39.9 months with NSAI plus goserelin; HR= 0.698 (95% CI: 0.462-1.054)] and a 20% reduction in the risk of death in MONALEESA-3 [median OS of 41.0 vs. 39.4 months with fulvestrant; HR=0.804 (95% CI: 0.596-1.083)].

In patients with liver metastases, Kisqali combination therapy showed a 47% reduction in the risk of death in MONALEESA-7 [median OS of NE vs. 33.6 months with NSAI plus goserelin; HR=0.531 (95% CI: 0.321-0.877)] and a 37% reduction in the risk of death in MONALEESA-3 [median OS of 36.1 vs. 24.1 months with fulvestrant; HR=0.629 (95% CI: 0.421-0.942)]. The adverse events were consistent with the overall

populations.

"Superior overall survival with Kisqali is proven in two phase III trials, and this subgroup analysis shows that Kisqali could make a difference in survival even among patients with the most aggressive forms of advanced breast cancer," said Susanne Schaffert, PhD, President, Novartis Oncology. "Patients are the inspiration behind everything we do, and we will continue to pursue bold treatment advancements that help reimagine the future for people with cancer in hopes that they can live longer, and better."

Additional Kisqali data presented during the ASCO20 Virtual Scientific Program include:

- An oral presentation on the largest pooled biomarker dataset of any CDK4/6 inhibitor in advanced breast cancer to date across a targeted panel of approximately 550 genes related to cancer and signaling pathways. The analysis identifies key potential gene alterations and their associations with response or resistance to Kisqali across all three MONALEESA trials⁴.
- Updated results from CompLEEmen-1, a Phase IIIb single-arm trial of 3,246 patients in first-line setting evaluating Kisqali plus letrozole in an expanded and diverse population closely resembling real-world clinical practice. Results were consistent with those observed in the MONALEESA trials, including median time to progression 27.1 months (95% CI: 25.7-NE) and overall response rate 43.6% (95% CI: 41.5-45.8%). The most common AEs were neutropenia, nausea and fatigue. Treatment-related AEs led to discontinuation in 12.9% of patients⁵.
- A retrospective study using real-world data assessing the economic burden of neutropenia, the most common adverse event following administration of CDK4/6 inhibitors. Neutropenia was reported in 38 patients (25%) in the palbociclib group and 25 patients (17%) in the Kisqali group. Similar rates of neutropenia were observed for grades 1/2 and 4, however, a numerical difference was observed for grade 3: palbociclib 35% vs. Kisqali 26%⁶.

Visit <https://www.virtualcongress.novartis.com/ASCO20> for the latest information from Novartis, including our commitment to the Oncology community, and access to our ASCO20 Virtual Scientific Program data presentations (for registered participants).

Kisqali is approved for use in more than 75 countries around the world, including the United States and European Union member states. Kisqali has shown statistically significant overall survival benefit in two Phase III trials with two distinct patient populations^{7,8}.

About Kisqali® (ribociclib)

Kisqali is the CDK4/6 inhibitor with the largest body of first-line clinical trial evidence demonstrating consistent and sustained efficacy compared to endocrine therapy alone. Overall survival results from MONALEESA-7 and MONALEESA-3 were presented at ASCO 2019 and ESMO 2019 respectively, demonstrating Kisqali plus endocrine therapy significantly extends life in pre/perimenopausal or postmenopausal women with HR+/HER2- advanced breast cancer. Overall survival follow-up is ongoing for the Phase III MONALEESA-2 trial.

Kisqali was initially approved by the US Food and Drug Administration (FDA) in March 2017 and by the European Commission (EC) in August 2017, as initial endocrine-based therapy for postmenopausal women with HR+/HER2- locally advanced or metastatic breast cancer in combination with an aromatase inhibitor based on findings from the pivotal MONALEESA-2 trial. Kisqali in combination with an aromatase inhibitor was approved for the treatment of pre-, peri- or postmenopausal women as initial endocrine based therapy, and also indicated for use in combination with fulvestrant as both first- or second-line therapy in postmenopausal women by the FDA in July 2018 and by the EC in December 2018. Regulatory filings are underway with other health authorities worldwide.

Novartis is continuing to reimagine cancer by investigating Kisqali in early breast cancer. The NATALEE study is a Phase III clinical trial of Kisqali with endocrine therapy in the adjuvant treatment of HR+/HER2- early breast cancer being conducted in collaboration with Translational Research In Oncology (TRIO).

Kisqali was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals.

About Novartis in Advanced Breast Cancer

Novartis tackles breast cancer with superior science, collaboration and a passion for transforming patient care. We've taken a bold approach to our research by including patient populations often neglected in clinical trials, identifying new pathways or mutations that may play a role in disease progression and developing therapies that not only maintain, but also improve, quality of life for patients. Our priority over the past 30 years and today is to deliver treatments proven to improve and extend lives for those diagnosed with advanced breast cancer.

Indication

KISQALI® (ribociclib) is a prescription medicine used in combination with an aromatase inhibitor for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2-) advanced or metastatic breast cancer, as initial endocrine-based therapy; or fulvestrant for the treatment of postmenopausal women with HR+/HER2- advanced or metastatic breast cancer, as initial endocrine-based therapy or following disease progression on endocrine therapy.

Important Safety Information

KISQALI can cause severe or life-threatening inflammation of the lungs. Patients should tell their health care provider right away if they experience breathing problems or chest pains. KISQALI can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. KISQALI is not indicated for concomitant use with tamoxifen due to an increased risk of QT prolongation. Patients should tell their health care provider right away if they have a change in their heartbeat (a fast or irregular heartbeat), or if they feel dizzy or faint. KISQALI can cause serious liver problems. Patients should tell their health care provider right away if they get any of the following signs and symptoms of liver problems: yellowing of the skin or the whites of the eyes (jaundice), dark or brown (tea-colored) urine, feeling very tired, loss of appetite, pain on the upper right side of the stomach area (abdomen), and bleeding or bruising more easily than normal. Low white blood cell counts are very common when taking KISQALI and may result in infections that may be severe. Patients should tell their health care provider right away if they have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Before taking KISQALI, patients should tell their health care provider if they are pregnant, or plan to become pregnant as KISQALI can harm an unborn baby. Females who are able to become pregnant and who take KISQALI should use effective birth control during treatment and for at least 3 weeks after the last dose of KISQALI. Do not breastfeed during treatment with KISQALI and for at least 3 weeks after the last dose of KISQALI.

Patients should tell their health care provider about all of the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements since they may interact with KISQALI. Patients should avoid grapefruit or grapefruit juice while taking KISQALI.

The most common side effects (incidence $\geq 20\%$) include white blood cell count decreases, nausea, infections,

tiredness, diarrhea, vomiting, hair loss, headache, constipation, rash, and cough. The most common grade 3/4 side effects (incidence >5%) were low neutrophils, low leukocytes, abnormal liver function tests, and low lymphocytes. Abnormalities were observed in hematology and clinical chemistry laboratory tests.

Please see full Prescribing Information for KISQALI, available at www.kisqali.com.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs about 15,000 people in the United States. For more information, please visit <http://www.novartis.us>.

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References

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