THE MONALEESA CLINICAL TRIAL PROGRAM

KISQALI® (ribociclib) offers a chance for more life to those affected by HR+/HER2- metastatic breast cancer, which is the most common subtype of metastatic breast cancer.[1]

The MONALEESA clinical trial program established KISQALI as the only CDK4/6 inhibitor with proven overall survival (OS) benefit across 3 phase 3 trials with multiple treatment combination partners, regardless of menopausal status or line of therapy.[2-4] MONALEESA-7, -3, and -2 are randomized phase 3 trials dedicated to evaluating KISQALI in women with HR+/HER2- metastatic breast cancer (MBC), which showed the longest median overall survival ever reported in **HR+/HER2- MBC**.[5]

The Unmet Need in Metastatic Breast Cancer

Breast cancer recently became the most commonly diagnosed cancer in the world, and an estimated **361,826** **ARE DIAGNOSED WITH METASTATIC BREAST CANCER EACH YEAR AROUND THE GLOBE.**[6-8]

Overall survival, a clinical trial end point, is the total length of time after someone begins treatment that he or she continues to live. In a clinical trial, it is a direct way to see if a treatment helped people live longer compared to another treatment. In other terms, it's about **adding more days to a person's life**.

	MONALEESA-7	MONALEESA-3	MONALEESA-2
ABOUT THE TRIAL **The primary end point of the MONALEESA clinical trial program was progression-free survival. The secondary end point was overall survival.*	• **KISQALI** + endocrine therapy vs placebo + endocrine therapy as first-line treatment for premenopausal women with HR+/HER2- advanced breast cancer • **672** women enrolled[3]	• **KISQALI** + fulvestrant vs placebo + fulvestrant as first- or second-line treatment for postmenopausal women with HR+/HER2- advanced breast cancer • **726** women enrolled[4]	• **KISQALI** + letrozole vs placebo + letrozole as first-line treatment for postmenopausal women with HR+/HER2- advanced breast cancer • **668** women enrolled[2]
OVERALL SURVIVAL	• **KISQALI** + endocrine therapy in the intent-to-treat population demonstrated statistically significant overall survival results compared to placebo + endocrine therapy (**HR=0.71**; *P*=0.00973).[3] • Overall survival at 42 months[3]: » **70%** for women who received **KISQALI** + endocrine therapy vs **46%** for women who received placebo + endocrine therapy	• **KISQALI** + fulvestrant demonstrated statistically significant overall survival results compared to placebo + fulvestrant (**HR=0.72**; *P*=0.00455).[4] • Overall survival at 42 months[4]: » **58%** for women who received **KISQALI** combination treatment vs **46%** for women who received placebo + fulvestrant	• **KISQALI** + letrozole demonstrated statistically significant overall survival benefit compared to placebo + letrozole (**HR=0.76**; *P*=0.004).[2] • Estimated six-year overall survival rate[2]: » **44.2%** for women who received **KISQALI** + letrozole vs. **32.0%** for women who received placebo + letrozole
MEDIAN OVERALL SURVIVAL	• **KISQALI + NSAI + goserelin subgroup** had a median overall survival of 58.7 months compared to placebo + endocrine therapy.[9] • Median OS *(not prespecified)*[9]: » **58.7 months** for women who received **KISQALI** + endocrine therapy vs **48 months** for women who received placebo + endocrine therapy (**HR=0.76** [95% CI, 0.61-0.96])	• **KISQALI + fulvestrant** had a median overall survival of 53.7 months compared to placebo + fulvestrant.[10] • Median OS *(not prespecified)*[10]: » **53.7 months** for women who received **KISQALI** + fulvestrant vs **41.5 months** for women who received placebo + fulvestrant (**HR=0.73** [95% CI, 0.59-1.04])	• **KISQALI + letrozole** had a median overall survival of 63.9 months compared to placebo + letrozole.[2] • Median OS *(prespecified)*[2]: » **63.9 months** for women who received **KISQALI** + letrozole vs **51.4 months** for women who received placebo + letrozole (**HR=0.76** [95% CI, 0.63-0.93])
SAFETY	• **KISQALI** is not indicated for use with tamoxifen. In the subgroup of women who received tamoxifen, an increased risk for QT prolongation was observed. • Most common grade 3/4 AEs for **KISQALI** combination therapy vs placebo + endocrine therapy[3]: » **Neutropenia** (63.5% vs 4.5%) » **Hepatobiliary toxicity** (11% vs 6.8%) • Discontinuation rate due to AEs: **3.3%** (**KISQALI** combination therapy) vs **3.9%** (placebo + endocrine therapy)[3]	• Most common grade 3/4 AEs for **KISQALI** + fulvestrant vs placebo + fulvestrant[4]: » **Neutropenia** (57.1% vs 0.8%) » **Leukopenia** (15.5% vs 0%) • Discontinuation rate due to AEs: **8.9%** (**KISQALI** + fulvestrant) vs **3.7%** (placebo + fulvestrant)[4]	• Most common grade 3/4 AEs for **KISQALI** + letrozole vs placebo + letrozole[2]: » **Neutropenia** (63.8% vs 1.2%) » **Hepatobiliary toxicity** (14.4% vs 4.8%) • Discontinuation rate due to AEs: **11.1%** (**KISQALI** + letrozole) vs **2.7%** (placebo + letrozole)[2]

THE MONALEESA CLINICAL TRIAL PROGRAM

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about KISQALI?

KISQALI may cause serious side effects, including:

Lung problems. KISQALI may cause severe or life-threatening inflammation of the lungs during treatment that may lead to death. Tell your health care provider right away if you have any new or worsening symptoms, including:

- trouble breathing or shortness of breath
- cough with or without mucus
- chest pain

Severe skin reactions. Tell your health care provider or get medical help right away if you get severe rash or rash that keeps getting worse; reddened skin; flu-like symptoms; skin pain/burning; blistering of the lips, eyes, or mouth; or blisters on the skin or skin peeling, with or without fever.

Heart rhythm problems (QT prolongation). KISQALI can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. Your health care provider should check your heart and do blood tests before and during treatment with KISQALI. Tell your health care provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you feel dizzy or faint.

Liver problems (hepatobiliary toxicity). KISQALI can cause serious liver problems. Your health care provider should do blood tests to check your liver before and during treatment with KISQALI. Tell your health care provider right away if you get any of the following signs and symptoms of liver problems:

- yellowing of your skin or the whites of your eyes (jaundice)
- dark or brown (tea-colored) urine
- feeling very tired
- loss of appetite
- pain on the right side of your stomach area (abdomen)
- bleeding or bruising more easily than normal

Low white blood cell counts (neutropenia). Low white blood cell counts are very common when taking KISQALI and may result in infections that may be severe. Your health care provider should check your white blood cell counts before and during treatment with KISQALI. Tell your health care provider right away if you have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Your health care provider may tell you to decrease your dose, temporarily stop, or completely stop taking KISQALI if you develop certain serious side effects during treatment with KISQALI.

What should I tell my health care provider before taking KISQALI?

Before you take KISQALI, tell your health care provider if you:

- have any heart problems, including heart failure, irregular heartbeats, and QT prolongation
- have ever had a heart attack
- have a slow heartbeat (bradycardia)
- have problems with the amount of potassium, calcium, phosphorus, or magnesium in your blood
- have fever, chills, or any other signs or symptoms of infection
- have liver problems
- have any other medical conditions
- are pregnant, or plan to become pregnant. KISQALI can harm your unborn baby
  - If you are able to become pregnant, your health care provider should do a pregnancy test before you start treatment with KISQALI.
  - 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.
  - Talk to your health care provider about birth control methods that may be right for you during this time.
  - If you become pregnant or think you are pregnant, tell your health care provider right away.
- are breastfeeding or plan to breastfeed. It is not known if KISQALI passes into your breast milk. Do not breastfeed during treatment with KISQALI and for at least 3 weeks after the last dose of KISQALI

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. KISQALI and other medicines may affect each other, causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

What should I avoid while taking KISQALI?

Avoid eating grapefruit and avoid drinking grapefruit juice during treatment with KISQALI since these may increase the amount of KISQALI in your blood.

The most common side effects of KISQALI include:

- neutropenia
- nausea
- infections
- fatigue
- diarrhea
- leukopenia
- vomiting
- hair loss
- headache
- constipation
- rash
- cough

KISQALI may cause fertility problems if you are male and take KISQALI. This may affect your ability to father a child. Talk to your health care provider if this is a concern for you.

Tell your health care provider if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of KISQALI. For more information, ask your health care provider or pharmacist. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

REFERENCES

THE MONALEESA CLINICAL TRIAL PROGRAM

References

1. American Cancer Society. Breast cancer facts and figures 2019-2020. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2019-2020.pdf. Accessed January 20, 2021.
2. Hortobagyi GN, et al. Updated overall survival (OS) results from the phase III MONALEESA-2 trial of postmenopausal women with HR+/HER2- advanced breast cancer (ABC) treated with letrozole ± ribociclib (RIB). Presented at the European Society for Medical Oncology (ESMO) Annual Meeting; September 16-21, 2021: Virtual. Abstract LBA17.
3. Im S-A, et al. Overall survival with ribociclib plus endocrine therapy in breast cancer. *N Engl J Med.* 2019;381:307-316.
4. Slamon DJ, Neven P, Chia S, Fasching PA, De Laurentiis M, Im S-A, et al. Overall survival with ribociclib plus fulvestrant in advanced breast cancer. *N Engl J Med.* 2020;382(6):514-524.
5. Novartis Pharmaceuticals Corporation. Data on file. August 26, 2021.
6. Globocan 2020 (WHO). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21660. Accessed February 23, 2021.
7. Gheorghe D. Breast Cancer Disease Landscape & Forecast 2017. https://clarivate.com/products/research-reports/report/dlsfon0001-2017-biopharma-breast-cancer-disease-landscape-and-forecast/. Accessed September 13, 2021.
8. Globocan 2020 (WHO). Cancer today: estimated number of new cases in 2020, worldwide, females, all ages, 2020. https://gco.iarc.fr/today/online-analysis-multi-bars?v=2020&mode=cancer&mode_population=countries&population=900&populations=900&key=asr&sex=2&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=10&group_cancer=1&include_nmsc=1&include_nmsc_other=1&type_multiple=%257B%2522inc%2522%253Atrue%252C%2522mort%2522%253Afalse%252C%2522prev%2522%253Afalse%257D&orientation=horizontal&type_sort=0&type_nb_items=%257B%2522top%2522%253Atrue%252C%2522bottom%2522%253Afalse%257D. Accessed September 9, 2021.
9. Tripathy D, Im S-A, Colleoni M, et al. Updated overall survival (OS) results from the phase III MONALEESA-7 trial of pre- or perimenopausal patients with HR+/HER2− advanced breast cancer (ABC) treated with endocrine therapy (ET) ± ribociclib. Presented at the San Antonio Breast Cancer Symposium; December 9, 2020: San Antonio, Texas. Abstract PD2-04.
10. Slamon D, Neven P, Chia S, et al. Updated overall survival (OS) results from the phase III MONALEESA-3 trial of postmenopausal patients (pts) with HR+/HER2− advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 5, 2021: Chicago, Illinois. Abstract 1001.

NOVARTIS

Novartis Pharma AG
CH-4002 Basel Switzerland

09/21 119616-1

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080