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MEDIA UPDATE

NEJM publication of Novartis Kisqali® data shows longest median overall survival ever reported in HR+/HER2- advanced breast cancer

- *MONALEESA-2 results show a statistically significant more than one-year increase in survival for women with HR+/HER2- postmenopausal aBC when using Kisqali plus letrozole compared to letrozole alone as first-line therapy*[1]
- *Kisqali plus letrozole achieved a median overall survival (OS) of over five years (63.9 months), with OS benefit increasing over time*[1]
- *NCCN guidelines recognize Kisqali as the only CDK4/6 inhibitor with OS benefit in first-line HR+/HER2- aBC based on these results*[2]
- *Kisqali is the only CDK4/6 inhibitor with consistent OS benefit across all three Phase III trials, regardless of menopausal status, site and number of metastases, prior treatment, endocrine partner, or line of therapy*[1,3-10]

Basel, March 9, 2022 — Novartis today announced that *The New England Journal of Medicine* (NEJM) published data showing the Phase III MONALEESA-2 trial for Kisqali® (ribociclib) plus letrozole demonstrated a statistically significant improvement in overall survival. The data show more than a 12 month increase in overall survival for Kisqali plus letrozole compared to letrozole alone, in postmenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer[1]. MONALEESA-2 overall survival data were first presented at the European Society for Medical Oncology (ESMO) Congress in September 2021[3]. The *NEJM* publication includes additional analyses substantiating the longest median overall survival benefit ever reported for HR+/HER2- advanced breast cancer patients, supporting the use of Kisqali combination therapy as a first-line treatment[1].

“These positive MONALEESA-2 overall survival data mark tremendous progress in extending the lives of patients living with advanced breast cancer. Achieving overall survival is the gold standard of clinical trials and is particularly impressive in the first-line setting,” said Gabriel N. Hortobagyi, MD, FACP, Professor of Medicine, University of Texas MD Anderson Cancer Center. “Despite higher subsequent use of CDK4/6 inhibitor therapy in the placebo arm, the ribociclib treatment arm demonstrated a statistically significant overall survival benefit of more than one year. These data solidify ribociclib and letrozole as the preferred CDK4/6 inhibitor combination to offer postmenopausal women with HR+/HER2- advanced disease more time.”

The *NEJM* publication includes the following findings:

- Median overall survival among patients in the Kisqali plus letrozole group was over five years (63.9 months) compared to four years (51.4 months) for the placebo group (HR=0.76; 95% CI: 0.63-0.93; two-sided p=0.008)[1].
- Patients who received Kisqali plus letrozole as first-line therapy saw a 24% reduction in risk of death compared to those receiving letrozole alone[1].

- The overall survival benefit with Kisqali plus letrozole continued to increase over time, with the survival rate of patients receiving Kisqali plus letrozole at 52.3% at five years (8.4% higher than letrozole alone) and 44.2% at six years (12.2% higher than letrozole alone)[1].
- Fewer patients in the Kisqali plus letrozole group received subsequent treatment with any-line CDK4/6 inhibitor therapy (34.4% for letrozole alone compared to 21.7%); the significant overall survival benefit with Kisqali plus letrozole was consistent after adjusting for subsequent treatment with any-line CDK4/6 inhibitors[1].
- Patients on Kisqali plus letrozole compared to those on letrozole alone experienced an additional one-year delay to subsequent chemotherapy (50.6 months compared to 38.9 months in the placebo group)[1].
- This study has the longest reported follow-up for any CDK4/6 inhibitor clinical trial to date with a median of 80 months, with no new safety signals emerging; adverse events were consistent with previously reported Phase III trial results for Kisqali[1].

“What’s most compelling about these MONALEESA-2 data is to see that the overall survival benefit of Kisqali plus letrozole was improving over time for patients, regardless of disease characteristics. These meaningful outcomes are elevating the standard of care for people living with advanced breast cancer, who now have hope for a longer quality life,” said Susanne Schaffert, PhD, President, Novartis Oncology. “Data continue to show that Kisqali sets itself apart from other CDK4/6 inhibitors, and we look forward to continue studying all its potential benefits for patients living with HR+/HER2- breast cancer.”

Further sub-analyses from these data will be shared with the scientific community later this year. The *NEJM* publication of the full data results is available online at www.NEJM.org (doi:10.1056/NEJMoa2114663) with an accompanying video and one-page summary. The MONALEESA-2 overall survival data from ESMO Congress 2021 are featured in a media release[3].

About Kisqali® (ribociclib)
Kisqali is the only CDK4/6 inhibitor with proven overall benefit across all three Phase III advanced trials[1,3-7], and is recognized by the National Comprehensive Cancer Network (NCCN) guidelines as the only CDK4/6 inhibitor with overall survival benefit in first-line HR+/HER2- advanced breast cancer[2]. Additionally, Kisqali has the highest rating of any CDK4/6 inhibitor on the ESMO Magnitude of Clinical Benefit Scale, achieving a score of five out of five for first-line premenopausal patients with HR+/HER2- advanced breast cancer[10].

Kisqali is a unique CDK4/6 inhibitor with the largest body of clinical trial evidence demonstrating consistent and superior overall survival benefit compared to endocrine therapy alone. Overall survival results were presented previously: MONALEESA-7 (American Society of Clinical Oncology [ASCO] 2019), MONALEESA-3 (ESMO 2019) and MONALEESA-2 (ESMO 2021); MONALEESA-7, MONALEESA-3 and MONALEESA-2 were published in The *NEJM*, with updated exploratory analyses presented at San Antonio Breast Cancer Symposium (SABCS) 2020, ASCO 2021 and SABCS 2021, demonstrating Kisqali plus endocrine therapy significantly extends life in pre/perimenopausal or postmenopausal patients with HR+/HER2- advanced breast cancer compared to endocrine therapy alone[1,3-9].

Kisqali has been approved in more than 95 countries worldwide, including by the United States Food and Drug Administration (FDA) and the European Commission, for the treatment of women with HR+/HER2- advanced or metastatic breast cancer in combination either with an aromatase inhibitor or with fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy[11-12]. Kisqali in combination with fulvestrant is approved as initial endocrine-based therapy or following disease progression on endocrine therapy in men by the FDA[11].

Novartis is continuing to reimagine cancer with additional trials of Kisqali. NATALEE is a large confirmatory 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)[12].

The unique profile of Kisqali and its overall survival benefit support rationale for HARMONIA, the first prospective, head-to-head Phase III trial seeking to identify the best therapeutic option between Kisqali and Ibrance®* for patients with advanced HR+/HER2-, HER2-enriched subtype which usually face worse prognosis. Novartis is collaborating with SOLTI, who is leading HARMONIA to test the hypothesis whether Kisqali changes tumor biology to enable a better response to endocrine-based therapy, affecting the course of HR+/HER2- disease.

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

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

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 may improve, quality of life for patients. Our priority over the past 30 years and today is to deliver treatments proven to improve the lives of those diagnosed with advanced breast cancer.

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About Novartis
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 products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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References

1. Hortobagyi, et al. Overall Survival With Ribociclib Plus Letrozole in Advanced Breast Cancer. N Engl J Med 2022; 386:942-50.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) – Breast Cancer. Version 1.2022.
3. Hortobagyi, et al. Overall survival (OS) results from the phase III MONALEESA (ML)-2 trial of postmenopausal patients with hormone receptor positive/human epidermal growth factor receptor 2 negative (HR+/HER2−) advanced breast cancer (ABC) treated with endocrine therapy (ET) ± ribociclib. Presented at the European Society of Medical Oncology (ESMO) Congress, September 16-21, 2021, (Abstract #LBA17).
4. Im, S. A. et al. Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer. N Engl J Med 2019; 381:307-316.
5. 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):514–24.
6. 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, (Abstract #1001).
7. 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. Abstract #PD2-04.
8. Yardley, Denise, A. et. al. Overall survival (OS) in patients (pts) with advanced breast cancer (ABC) with visceral metastases (mets), including those with liver mets, treated with ribociclib (RIB) plus endocrine therapy (ET) in the MONALEESA (ML) -3 and -7 trials. Presented at the American Society of Clinical Oncology (ASCO) meeting (Abstract #1054).
9. O'Shaughnessy J et al. Overall survival subgroup analysis by metastatic site from the Phase III MONALEESA-2 study of first-line ribociclib + letrozole in postmenopausal patients with HR+/HER2− advanced breast cancer. Presented at the San Antonio Breast Cancer Symposium, December 7-10, 2021. Abstract #GS2-01.
10. European Society for Medical Oncology – Magnitude of Clinical Benefit Scale Score Card. https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-scorecards/scorecard-158-1. Published April 20, 2020. Updated August 21, 2020. Accessed September 9, 2020.
11. Kisqali (ribociclib) Prescribing Information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation; July 2020.
12. Novartis Pharmaceuticals and Translational Research in Oncology (2018, December 7 – 2026, May 29). A Trial to Evaluate Efficacy and Safety of Ribociclib With Endocrine Therapy as Adjuvant Treatment in Patients With HR+/HER2- Early Breast Cancer (NATALEE). Identifier NCT03701334. https://clinicaltrials.gov/ct2/show/NCT03701334.
13. Novartis Data on File. Novartis Pharmaceuticals Corp: 2021.

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