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MEDIA UPDATE

Novartis Kisqali® reduced the risk of cancer recurrence while maintaining quality of life in patients diagnosed with early breast cancer

- *Patient-reported outcomes (PROs) from the Phase III NATALEE trial show that patients receiving adjuvant Kisqali plus endocrine therapy (ET) for up to three years maintained physical and social functioning; psychological well-being; and overall health scores, compared to baseline*[1]

- *Health-related quality of life scores (HRQoL) were also comparable between patients treated with Kisqali plus ET and those treated with ET alone, suggesting that Kisqali reduced the risk of cancer recurrence without adding to the burden of care*[1]

Basel, September 14, 2023 — Novartis today presents new patient-reported outcomes (PRO) data from the Phase III NATALEE trial at the European Society for Medical Oncology (ESMO) Virtual Plenary. The data show that a broad population of patients with stage II and III hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC) maintained health-related quality of life (HRQoL) during treatment with Kisqali® (ribociclib) plus endocrine therapy (ET)[1].

“Treatment in early breast cancer is physically and emotionally arduous, and afterwards people diagnosed with EBC struggle to balance the worry of their cancer returning with the burden of managing adjuvant treatment,” said Dr. Peter A. Fasching, Professor of Gynecology and Obstetrics Translational Medicine, at the University Hospital Erlangen and Comprehensive Cancer Center Erlangen-EMN and NATALEE trial investigator. “The patient-reported outcomes from NATALEE reinforce Kisqali as a potential adjuvant option that reduces the risk of cancer returning without compromising patients’ well-being, mental health or physical abilities.”

Patients treated with Kisqali plus ET for up to three years maintained their physical functioning and global health scores when compared to both their baseline scores and to patients treated with ET alone, demonstrating that patients maintained their overall HRQoL when treated with adjuvant Kisqali[1].

“No patient should have to choose between maintaining their quality of life and doing everything they can to remain cancer free,” said Jeff Legos, Executive Vice President, Global Head of Oncology and Hematology Development at Novartis. “These patient-reported outcomes add to the wealth of efficacy and tolerability data from the NATALEE trial suggesting Kisqali is a potential adjuvant treatment of choice for a broad range of patients

with HR+/HER2- EBC, including those with node-negative disease. Kisqali could enable patients with EBC to live well with greater peace of mind."

Further analysis of the NATALEE trial is ongoing, and additional data will be shared at upcoming medical meetings.

About NATALEE
NATALEE is a global Phase III multi-center, randomized, open-label trial to evaluate the efficacy and safety of Kisqali with ET as adjuvant treatment versus ET alone in patients with HR+/HER2- EBC, being conducted in collaboration with TRIO[2]. The adjuvant ET in both treatment arms was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin if applicable[2]. The primary endpoint of NATALEE is iDFS as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria[2]. A total of 5,101 adult patients with HR+/HER2- EBC across 20 countries were randomized in the trial[2].

Results showed Kisqali plus ET, compared to ET alone, lowered the risk of cancer recurrence by 25.2% (HR=0.748; 95% CI: 0.618, 0.906; p=0.0014), along with consistent clinically meaningful iDFS benefit across key pre-specified subgroups: AJCC Tumor Stage II (HR=0.761; 95% CI: 0.525, 1.103), AJCC Tumor Stage III (HR=0.740; 95% CI: 0.592, 0.925), node-negative disease (HR=0.630; 95% CI: 0.341, 1.165), node-positive disease (HR=0.771; 95% CI: 0.630, 0.944), pre-menopausal women and men (HR=0.722; 95% CI: 0.530, 0.983), post-menopausal women (HR=0.781; 95% CI: 0.613, 0.997)[2]. Kisqali data across all secondary efficacy endpoints was also consistent, including DDFS (26% risk reduction) and RFS (28% risk reduction), with a trend for improvement in OS (HR=0.759; 95% CI: 0.539, 1.068)[*2].

Median study duration of follow up was 34 months (range 21-48 months) with clinical benefits observed after approximately two years[2]. NATALEE explored a lower starting dose (400 mg) of Kisqali than the dose approved for treatment in metastatic breast cancer (MBC) (600 mg) with the goal to minimize disruptions to patient quality of life without compromising efficacy. The safety profile of Kisqali at 400 mg was favorable with low rates of symptomatic AEs and limited need for dose modifications when administered up to three years[2]. The most frequently reported AEs of special interest (grade 3 or higher) were neutropenia (43.8%) and liver-related AEs (e.g. elevated transaminases) (8.3%)[2].

**Results based on pre-specified interim analysis for OS at time of primary iDFS analysis; additional follow up is planned to obtain more mature OS data[2].*

About Early Breast Cancer
More than 90% of patients diagnosed with breast cancer have EBC[3]. Despite standard-of-care adjuvant therapy, approximately one-third of those diagnosed with stage II and more than half of those diagnosed with stage III HR+/HER2- EBC experience cancer recurrence[4,5]. The risk of recurrence continues over decades with more than half of breast cancer recurrences occurring five or more years after diagnosis[4,6]. For many of these patients, there are currently no targeted therapeutic options outside of the standard chemotherapy and ET[7].

About Kisqali® (ribociclib)
Kisqali has consistently demonstrated OS benefit while preserving or improving quality of life across three Phase III trials in MBC[8-19]. Updates to the NCCN Guidelines® for breast cancer, released in January 2023, recommend ribociclib (Kisqali) as the only Category 1 preferred CDK4/6 inhibitor for first-line treatment of patients with HR+/HER2- MBC when combined with an aromatase inhibitor (AI)[20]. 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 pre-menopausal patients with HR+/HER2- advanced breast cancer[21]. Further, Kisqali in combination with either letrozole or fulvestrant has uniquely, among other CDK4/6

inhibitors, received a score of four out of five for post-menopausal patients with HR+/HER2- advanced breast cancer treated in the first line[22].

Kisqali has been approved in 99 countries worldwide, including by the United States Food and Drug Administration (FDA) and the European Commission. In the U.S., Kisqali is approved for the treatment of adult patients with HR+/HER2- advanced or MBC in combination with an AI as initial ET or fulvestrant as initial ET or following disease progression on ET in post-menopausal women or in men. In the EU, Kisqali is approved for the treatment of women with HR+/HER2- advanced or MBC in combination with either an AI or fulvestrant as initial ET or following disease progression. In pre- or peri-menopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist[19].

Novartis is committed to continuing to study Kisqali in breast cancer. Novartis is collaborating with SOLTI, which is leading the HARMONIA study to test whether Kisqali changes tumor biology to enable a better response to ET compared to Ibrance®** (palbociclib) for patients with HR+/HER2-, HER2-enriched subtype[23] MBC, and with the Akershus University Hospital in Norway on the NEOLETRIB trial, a neoadjuvant Phase II trial studying the effects of Kisqali in HR+/HER2- EBC to discover the potentially unique underlying mechanism of action[24].

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

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References

1. Fasching P, Slamon D et al. Health-related quality of life in the phase 3 NATALEE study of adjuvant ribociclib plus a NSAI vs NSAI alone in patients with HR+/HER2− early breast cancer). Presentation at European Society for Medical Oncology (ESMO) Virtual Plenary on 14 September 2023.
2. Slamon D, Stroyakovskiy D, Yardley D, et al. Ribociclib and endocrine therapy as adjuvant treatment in patients with HR+/HER2− early breast cancer: primary results from the Phase III NATALEE trial. Presented at the American Society of Clinical Oncology Annual Meeting, June 2, 2023. Chicago, USA.
3. Iqbal J, Ginsburg O, Rochon PA, Sun P, Narod SA. Differences in breast cancer stage at diagnosis and cancer-specific survival by race and ethnicity in the United States [published correction appears in *JAMA*. 2015 Jun 9;313(22):2287]. *JAMA*. 2015;313(2):165-173. doi:10.1001/jama.2014.17322
4. Pan H, Gray R, Braybrooke J, et al; EBCTCG. 20-year risks of breast-cancer recurrence after stopping endocrine therapy at 5 years. *N Engl J Med*. 2017;377(19):1836-1846. doi:10.1056/NEJMoa1701830
5. Pan H, Gray R, Braybrooke J, et al; EBCTCG. 20-year risks of breast-cancer recurrence after stopping endocrine therapy at 5 years. *N Engl J Med*. 2017;377(19):1836-1846;(suppl). doi:10.1056/NEJMoa1701830
6. Gomis R, Gawrzak S. Tumor cell dormancy. Mol Oncol. 2017;11(1):62-78.
7. American Cancer Society. Treatment of breast cancer stages I-III. Revised April 12, 2022. Available at: https://www.cancer.org/cancer/breast-cancer/treatment/treatment-of-breast-cancer-by-stage/treatment-of-breast-cancer-stages-i-iii.html/ Accessed August 2023.
8. Yardley DA, Yap YS, et al. Pooled exploratory analysis of survival in patients (pts) with HR+/HER2- advanced breast cancer (ABC) and visceral metastases (mets) treated with ribociclib (RIB) + endocrine therapy (ET) in the MONALEESA (ML) trials. Poster presented at the European Society of Medical Oncology Congress. September 9-13, 2022. Paris, France.
9. Neven P, Fasching PA, et al. Updated overall survival (OS) results from the first-line (1L) population in the Phase III MONALEESA-3 trial of postmenopausal patients with HR+/HER2- advanced breast cancer (ABC) treated with ribociclib (RIB) + fulvestrant (FUL). Mini oral presented at the European Society for Medical Oncology Breast Cancer Congress. May 4, 2022. Paris, France.
10. Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer. *New England Journal of Medicine*. 2022;386(10):942-950. doi:10.1056/NEJMoa2114663
11. Hortobagyi GN, 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. Proffered paper presented at the European Society of Medical Oncology Congress, September 16-21, 2021. Lugano, Switzerland.
12. Im S-A, Lu Y-S, Bardia A, et al. Overall survival with ribociclib plus endocrine therapy in breast cancer. *New England Journal of Medicine*. 2019;381(4):307-316. doi:10.1056/nejmoa1903765
13. Slamon DJ, Neven P, Chia S, et al. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. *New England Journal of Medicine*. 2020;382(6):514-524. doi:10.1056/NEJMoa1911149
14. Slamon DJ, Neven P, Chia S, et al. Overall survival (OS) results of the Phase III MONALEESA-3 trial of postmenopausal patients (pts) with hormone receptor–positive (HR+), human epidermal growth factor 2–negative (HER2−) advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). Presented at the European Society of Medical Oncology Congress, September 29, 2019, Barcelona, Spain.
15. 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 Annual Meeting, June 5, 2021. Chicago, USA.
16. 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. Texas, USA.
17. Yardley D, Nusch A, Yap YS, 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) Annual Meeting. June 2020. Chicago, USA.

18. O'Shaughnessy J, Stemmer SM, Burris HA, 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. Texas, USA.
19. Kisqali (ribociclib) Prescribing Information.
20. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) - Breast Cancer. NCCN Guidelines. Published March 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf/ Accessed August 2023.
21. European Society for Medical Oncology – Magnitude of Clinical Benefit Scale Scorecard. Published April 20, 2020. Updated August 21, 2020. Available at: https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-scorecards/scorecard-158-1/ Accessed August 2023.
22. European Society for Medical Oncology – Magnitude of Clinical Benefit Scale Scorecard. Published March 29, 2022. Available at: https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-scorecards/scorecard-9-1/ Accessed August 2023.
23. Ribociclib vs. palbociclib in patients with advanced breast cancer within the HER2-enriched intrinsic subtype (HARMONIA). Identifier NCT05207709. Revised April 4, 2022. Available at: https://clinicaltrials.gov/ct2/show/NCT05207709/ Accessed August 2023.
24. Novartis and Vestre Viken Hospital Trust (2022, April 1 – 2024, December 1). Neoadjuvant Treatment of Locally-advanced Breast Cancer Patients With Ribociclib and Letrozole (NEOLETRIB). Identifier NCT05163106. Available at: https://clinicaltrials.gov/ct2/show/NCT05163106/ Accessed August 2023.

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