Novartis data demonstrates consistent efficacy and tolerability of Kisqali® combination therapy in HR+/HER2- advanced breast cancer in patients with difficult-to-treat visceral disease

Dec 08, 2018

- -Subgroup analyses of three pivotal Phase III MONALEESA trials showed Kisqali plus endocrine therapy extended PFS in all patients with and without visceral involvement compared to endocrine therapy alone; consistent with the overall study populations[1]
- -In patients with visceral metastasis, increased PFS benefit was seen regardless of burden of disease (≤ 3 or > 3 lesions)[1]
- -Approximately 41% of postmenopausal women with HR+ advanced breast cancer will develop their first metastasis in visceral organs, such as the lungs or liver, which is often associated with a poor prognosis[2],[3]

EAST HANOVER, N.J., Dec. 8, 2018 /PRNewswire/ -- Novartis today announced data from subgroup analyses of the three pivotal Phase III MONALEESA trials showing that Kisqali® (ribociclib) plus endocrine therapy extended progression-free survival (PFS) compared to endocrine therapy alone, regardless of the presence of visceral metastases in pre-, peri- and postmenopausal women with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced breast cancer[1]. These data will be presented today at the San Antonio Breast Cancer Symposium (SABCS) (Abstract #P6-18-07).

"Nearly 60% of patients enrolled in the MONALEESA clinical trials had visceral metastases, and all benefited from treatment with ribociclib in combination with endocrine therapy," said Denise Yardley, MD, Principal Investigator, Sarah Cannon Research Institute. "These results, coupled with the NCCN and ABC4 recommended treatment guidelines for HR+ advanced breast cancer patients with visceral metastases, support the use of ribociclib combination therapy as a standard of care in this patient population."

In patients with visceral metastases, Kisqali plus endocrine therapy extended median PFS by 11.5 months in MONALEESA-2 (24.9 months vs 13.4 months) and 13.4 months in MONALEESA-7 (23.8 months vs 10.4 months) compared to endocrine therapy alone. Median PFS for patients with visceral metastases in the MONALEESA-3 trial still has not been reached compared to 16.5 months median PFS in patients receiving endocrine therapy alone[1].

Kisqali plus endocrine therapy demonstrated consistent efficacy across the MONALEESA trials in patients with and without visceral metastases. In patients with visceral metastases and measurable disease, the overall response rate (ORR) in patients who received Kisqali plus endocrine therapy compared to endocrine therapy alone was 53% vs 40% (MONALEESA-2), 50% vs 38% (MONALEESA-7) and 48% vs 31% (MONALEESA-3). Patients without visceral disease showed an ORR of 59% vs 35%, 52% vs 32% and 49% vs 39% in the respective MONALEEA-2, MONALEESA-7 and MONALEESA-3 trials[1].

"Patients living with HR+/HER2- advanced breast cancer who have visceral metastases often have a poorer prognosis and are at higher risk for treatment resistance and disease progression than those without," said

Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "These sub analyses reaffirm that it is critical to treat HR+ advanced breast cancer with a CDK4/6 combination therapy, such as Kisqali plus fulvestrant or an aromatase inhibitor, to give all patients, especially those with visceral metastases, the strongest option for delaying disease progression."

Adverse events for patients with visceral metastases were consistent with those observed in the overall study populations and generally manageable through dose interruptions or reductions[1].

About Kisqali® (ribociclib)

Kisqali® (ribociclib) is the CDK4/6 inhibitor with the largest body of first-line clinical trial evidence demonstrating consistent, superior and sustained efficacy compared to endocrine therapy alone[4].

Kisqali is a selective cyclin-dependent kinase inhibitor, a class of drugs that help slow the progression of cancer by inhibiting two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). These proteins, when over-activated, can enable cancer cells to grow and divide too quickly. Targeting CDK4/6 with enhanced precision may play a role in ensuring that cancer cells do not continue to replicate uncontrollably[4].

Kisqali was initially approved by the US Food and Drug Administration (FDA) in March 2017 and by the European Commission 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. In July 2018, Kisqali was approved by the FDA for the treatment of pre-, peri- or postmenopausal women in the US, and indicated for use in combination with fulvestrant as both first- or second-line therapy in postmenopausal women. In November 2018, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending an expanded indication for Kisqali based on the MONALEESA-3 and MONALEESA-7 data. Regulatory filings are underway with other health authorities worldwide[4].

Kisqali is approved for use in more than 70 countries around the world, including the United States and European Union member states. Kisqali is not currently approved for use in combination with fulvestrant or in premenopausal women in Europe. Kisqali was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals[4].

Novartis is continuing to reimagine cancer by investigating Kisqali in early breast cancer (EBC). The NATALEE study is a Phase III clinical trial of Kisqali with endocrine therapy in the adjuvant treatment of HR+/HER2- EBC being conducted in collaboration with Translational Research In Oncology (TRIO)[4].

About Novartis in Advanced Breast Cancer

For more than 30 years, Novartis has been tackling breast cancer with superior science, great collaboration and a passion for transforming patient care. With one of the most diverse breast cancer pipelines and one of the largest numbers of breast cancer compounds in development, Novartis leads the industry in discovery of new therapies and combinations, especially in HR+ advanced breast cancer, the most common form of the disease.

Kisqali® (ribociclib) Important US Safety Information

KISQALI® (ribociclib) is a prescription medicine used in combination with an aromatase inhibitor as the first hormonal-based therapy to treat pre/peri- and postmenopausal women and in combination with fulvestrant as the first hormonal-based therapy or following disease progression on hormonal therapy in postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer. It is not known if KISQALI is safe and effective in children. 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 ≥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.

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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 1 billion people globally and we are finding innovative ways to expand access to our latest treatments. About 125,000 people of more than 140 nationalities work at Novartis around the world. Novartis Pharmaceuticals Corporation, a US affiliate of Novartis, is located in East Hanover, NJ.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis and @NovartisCancer at https://twitter.com/novartiscancer
For Novartis multimedia content, please visit www.novartis.com/news/media-library
For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Yardley D, Chan A, Nusch, A et al. Ribociclib + endocrine therapy in patients with hormone receptor-positive, HER2-negative advanced breast cancer presenting with visceral metastases: Subgroup analysis of Phase III MONALEESA trials. Presented at the San Antonio Breast Cancer Symposium (SABCS) (Abstract #P6-18-07) on December 8, 2018.
2. National Cancer Institute. Dictionary of Cancer Terms. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/visceral. Accessed November 2018.
3. Harb, WA. Management of patients with hormone receptor–positive breast cancer with visceral disease: challenges and treatment options. Cancer Manag Res. 2015;7:37-46.
4. Novartis Data on File.

SOURCE Novartis
