Novartis data highlight efficacy of Piqray® in HR+/HER2- metastatic breast cancer with a PIK3CA driver mutation immediately post-CDK4/6i

Dec 10, 2021

- New data underscore efficacy of Piqray, even in those patients with a short treatment duration on prior CDK4/6i or with ESR1 mutations, biomarkers of endocrine resistance[1-5]
- Recent guideline updates support use of Piqray with fulvestrant for postmenopausal HR+/HER2- PIK3CA-mutated mBC patients immediately after failure on prior CDK4/6i treatment[6]
- Piqray works synergistically with fulvestrant across the PI3K and estrogen receptor pathways, respectively--remaining the only treatment specifically approved for mBC with a PIK3CA mutation, a known oncogenic driver of the disease[7-9]
- Five BYLieve presentations include data on longer-term follow-up and ESR1 mutations, which occur in up to 56% of patients with HR+/HER2- mBC[1-5,10-11]

EAST HANOVER, N.J., Dec. 10, 2021 /PRNewswire/ -- Novartis today announced new Piqray® (alpelisib) data indicating benefit across a broad range of patient and disease characteristics as seen in analyses from all three cohorts of BYLieve. BYLieve is an ongoing Phase II, open-label, 3-cohort non-comparative study evaluating Piqray with endocrine therapy including men and pre- and postmenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer (mBC) who have progressed on or after prior therapies, including CDK4/6 inhibitor plus endocrine therapy[1-5]. These data will be presented at the 2021 San Antonio Breast Cancer Symposium (SABCS) from December 7-10.

"The data from all three cohorts of the BYLieve study have value for the medical community and for the patients we care for with mBC, because these cohorts show a benefit from alpelisib in the post-CDK4/6i setting for patients with HR+/HER2- PIK3CA-mutated cancer," said Dr. Hope S. Rugo, Director, Breast Oncology and Clinical Trials Education, University of California San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center. "Beyond illustrating the efficacy and safety of alpelisib, regardless of the duration of prior CDK4/6i treatment, the data provide meaningful insights into how alpelisib may benefit different subgroups of patients."

Highlights from the BYLieve data presented at SABCS

- BYLieve Cohort A (P1-18-03): Updated safety and efficacy data after 18 months of follow-up showed median overall survival improvement of 26.4 months (95% CI: 21.0-30.5) for patients treated with Piqray plus fulvestrant immediately following CDK4/6i plus an AI[1]. The most common all-grade adverse events (AEs) (n=127) were diarrhea (63.8%), hyperglycemia (59.8%), nausea (46.5%) and rash (31.5%)[1].

- BYLieve Cohort C (PD13-05): The third and final BYLieve cohort included patients who received chemotherapy or endocrine therapy as immediate prior treatment, who could have received prior CDK4/6i as well[2].

- The primary endpoint was met with 48.7% (95% CI: 39.3%-58.2%) of patients alive and without disease progression at six months[2].
- Data confirm clinically relevant activity of Piqray as a targeted therapy for PIK3CA as a driver oncogene[2].
- No new safety signals were observed, with the most common all-grade AEs (n=126) being hyperglycemia (65.1%), diarrhea (52.4%), nausea (40.5%) and rash (38.9%)[2].

- BYLieve Cohorts A & B (P1-18-08; P5-13-03; PD15-01): Exploratory biomarker and post-hoc analyses demonstrated efficacy with Piqray plus fulvestrant/letrozole in CDK4/6i-resistant mBC, as seen in patients with early discontinuation of the prior CDK4/6i (Cohort A: ≤6 months median PFS of 12.0 months and >6 months median PFS of 6.2 months; HR=0.51; 95% CI: 0.29-0.89; Cohort B: ≤6 months median PFS of 5.9 months and >6 months median PFS of 5.6 months; HR=0.72; 95% CI: 0.45-1.18), supporting the use of Piqray plus endocrine therapy as an immediate next-line option in these patients[3]. Grade ≥3 AEs were experienced by 84.6% (n=22) and 66.0% (n=66) of patients in the ≤6 months and >6 months subgroups, respectively, in Cohort A and by 62.5% (n=20) and 72.5% (n=66) of patients in the ≤6 months and >6 months subgroups, respectively, in Cohort B[3].

Additionally, the exploratory ctDNA analysis from Cohorts A and B (median PFS of 7.3 months and 5.7 months in Cohorts A and Cohort B, respectively) found that Piqray was effective in the post-CDK4/6i setting regardless of endocrine therapy partner and tumor genomic profile and other mutations associated with CDK4/6i resistance[4]. Across the three cohorts no new safety signals were observed, even with longer exposure, as seen in Cohort A, confirming no cumulative toxicities with Piqray[1-3].

An estimated 361,826 people are diagnosed with mBC worldwide each year, and approximately 40% of those with HR+/HER2- subtype have a PIK3CA mutation, which is associated with a poor prognosis[8-9].

Visit https://www.hcp.novartis.com/virtual-congress/sabcs-2021/ for the latest information from Novartis, including our commitment to the Oncology community, and access to our SABCS Virtual Scientific Program data presentations (for registered participants).

About Piqray® (alpelisib)

Piqray is a kinase inhibitor developed for use in combination with fulvestrant for the treatment of postmenopausal women, and men, with HR+/HER2-, PIK3CA-mutated, advanced or metastatic breast cancer following progression on or after endocrine-based regimen[7]. Piqray is approved in 64 countries, including the US and European member states[12].

Novartis is continuing to reimagine cancer with additional trials of Piqray. EPIK-B5 will be a large Phase III clinical trial of Piqray in combination with fulvestrant to complement the SOLAR-1 study[13]. Novartis is also studying the potential of Piqray in triple negative breast cancer (TNBC) in the EPIK-B3 Phase III clinical trial, in advanced HER2+ breast cancer in the EPIK-B2 Phase III clinical trial and in ovarian cancer in the EPIK-O Phase III clinical trial[14-16].

Indication

PIQRAY® (alpelisib) tablets is a prescription medicine used in combination with the medicine fulvestrant to treat women who have gone through menopause and men who have hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer or breast cancer that has spread to other parts of the body (metastatic), with an abnormal phosphatidylinositol-3-kinase catalytic subunit alpha

(PIK3CA) gene, and whose disease has progressed on or after endocrine therapy. Your health care provider will test your cancer for an abnormal "PIK3CA" gene to make sure that PIQRAY is right for you. It is not known if PIQRAY is safe and effective in children.

Important Safety Information

Patients should not take PIQRAY if they have had a severe allergic reaction to PIQRAY or are allergic to any of the ingredients in PIQRAY.

PIQRAY may cause serious side effects. PIQRAY can cause severe allergic reactions. Patients should tell their health care provider or get medical help right away if they have trouble breathing, flushing, rash, fever, or fast heart rate during treatment with PIQRAY. PIQRAY can cause severe skin reactions. Patients should tell their health care provider or get medical help right away if they get severe rash or rash that keeps getting worse, reddened skin, flu-like symptoms, blistering of the lips, eyes or mouth, blisters on the skin or skin peeling, with or without fever. PIQRAY can cause high blood sugar levels (hyperglycemia). Hyperglycemia is common with PIQRAY and its complications can be severe. Health care providers will monitor patients' blood sugar levels before they start and during treatment with PIQRAY. Health care providers may monitor patients' blood sugar levels more often if they have a history of type 2 diabetes. Patients should tell their health care provider right away if they develop symptoms of hyperglycemia or its complications, including excessive thirst, dry mouth, urinating more often than usual or having a higher amount of urine than normal, increased appetite with weight loss, confusion, nausea, vomiting, fruity odor on breath, difficulty breathing, or dry or flushed skin. PIQRAY can cause lung problems (pneumonitis). Patients should tell their health care provider right away if they develop new or worsening symptoms of lung problems, including shortness of breath or trouble breathing, cough, or chest pain. Diarrhea is common with PIQRAY and can be severe. Severe diarrhea can lead to the loss of too much body water (dehydration) and kidney problems. Patients who develop diarrhea during treatment with PIQRAY should tell their health care provider right away.

Before taking PIQRAY, patients should tell their health care provider if they have a history of diabetes, skin rash, redness of skin, blistering of the lips, eyes or mouth, or skin peeling, are pregnant, or plan to become pregnant as PIQRAY can harm their unborn baby. Females who are able to become pregnant should use effective birth control during treatment with PIQRAY and for 1 week after the last dose. Do not breastfeed during treatment with PIQRAY and for 1 week after the last dose. Males with female partners who are able to become pregnant should use condoms and effective birth control during treatment with PIQRAY and for 1 week after the last dose. Patients should also read the full Prescribing Information of fulvestrant for important pregnancy, contraception, infertility, and lactation information.

Patients should tell their health care provider all of the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. PIQRAY 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.

The most common side effects of PIQRAY when used with fulvestrant are rash, nausea, tiredness and weakness, decreased appetite, mouth sores, vomiting, weight loss, hair loss, and changes in certain blood tests.

Please see full Prescribing Information for PIQRAY, available at www.piqray.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 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.

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 nearly 15,000 people in the United States. For more information, please visit https://www.novartis.us.

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References

1. Ciruelos EM et al. Alpelisib + fulvestrant in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), PIK3CA-mutated advanced breast cancer (ABC) previously treated with cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) + aromatase inhibitor (AI): 18-month follow-up of BYLieve Cohort A. Presented at the San Antonio Breast Cancer Symposium,

December 8, 2021. Abstract #P1-18-03.
2. Rugo HS et al. Alpelisib + fulvestrant in patients with PIK3CA-mutated, HR+, HER2- advanced breast cancer (ABC) who received chemotherapy or endocrine therapy (ET) as immediate prior treatment: BYLieve Cohort C primary results and exploratory biomarker analyses. Presented at the San Antonio Breast Cancer Symposium, December 10, 2021. Abstract #PD13-05.
3. Chia S et al. Effect of duration of prior cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) therapy (≤6 mo or >6 mo) on alpelisib benefit in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), PIK3CA-mutated advanced breast cancer (ABC) from BYLieve. Presented at the San Antonio Breast Cancer Symposium, December 8, 2021. Abstract # P1-18-08.
4. Juric D et al. Alpelisib + endocrine therapy (ET) in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), PIK3CA-mutated advanced breast cancer (ABC) previously treated with cyclin-dependent kinase 4/6 inhibitor (CDK4/6i): Biomarker analyses from the Phase II BYLieve study. Presented at the San Antonio Breast Cancer Symposium, December 8, 2021. Abstract #P5-13-03.
5. Turner N et al. Impact of ESR1 mutations on endocrine therapy (ET) plus alpelisib benefit in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), PIK3CA-mutated, advanced breast cancer (ABC) who progressed on or after prior cyclin-dependent kinase inhibitor (CDK4/6i) therapy in the BYLieve trial. Presented at the San Antonio Breast Cancer Symposium, December 10, 2021. Abstract #PD15-01.
6. Burstein HJ, Somerfield MR, Barton DL, et al: Endocrine treatment and targeted therapy for HR-positive, HER2-negative metastatic breast Cancer: ASCO Guideline update. J Clin Oncol. July 29, 2021.
7. Piqray (alpelisib) Prescribing Information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation; July 2021.
8. The Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. Nature. 2012;490(7418):61-70.
9. Mosele F, Stefanovska B, Lusque A, et al. Outcome and molecular landscape of patients with PIK3CA-mutated metastatic breast cancer. Ann Oncol. 2020;31(3):377-386.
10. Fribbens, C., et al. Tracking Evolution of Aromatase Inhibitor Resistance with Circulating Tumour DNA Analysis in Metastatic Breast Cancer. Ann Oncol. 2018;29(1):145-153. https://doi.org/10.1093/annonc/mdx483.
11. Dustin D, et al. ESR1 Mutations in Breast Cancer. Cancer. 2019;125(21):3714-3728, https://doi.org/10.1002/cncr.32345.
12. Novartis Data on File. Novartis Pharmaceuticals Corp: 2021.
13. Novartis Pharmaceuticals. Study to Assess the Efficacy and Safety of Alpelisib Plus Fulvestrant in Participants With HR-postitive (HR+), HER2-negative, Advanced Breast Cancer After Treatment With a CDK4/6 Inhibitor and an Aromatase Inhibitor: EPIK-B5 (October 27, 2021- November 27, 2026). Identifier: NCT05038735. https://www.clinicaltrials.gov/ct2/show/NCT05038735.
14. Novartis Pharmaceuticals. Study Assessing the Efficacy and Safety of Alpelisib + Nab-paclitaxel in Subjects With Advanced TNBC Who Carry Either a PIK3CA Mutation or Have PTEN Loss: EPIK-B3 (June 8, 2020-January 9, 2026). Identifier: NCT04251533. https://www.clinicaltrials.gov/ct2/show/NCT04251533.
15. Novartis Pharmaceuticals. EPIK-B2: A Two Part, Phase III, Multicenter, Randomized (1:1), Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of Alpelisib (BYL719) in Combination With Trastuzumab and Pertuzumab as Maintenance Therapy in Patients With HER2-positive Advanced Breast Cancer With a PIK3CA Mutation. Identifier: NCT04208178. https://www.clinicaltrials.gov/ct2/show/NCT04208178.
16. Novartis Pharmaceuticals. Alpelisib Plus Olaparib in Platinum-resistant/Refractory, High-grade Serous Ovarian Cancer, With no Germline BRCA Mutation Detected: EPIK-O (July 2, 2021-January 31, 2025).

Identifier: NCT04729387. https://www.clinicaltrials.gov/ct2/show/NCT04729387.

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