Novartis Piqray® - First and only treatment specially for patients with a PIK3CA mutation in HR+/HER2- advanced breast cancer receives HSA approval

Mar 01, 2021

- Piqray (alpelisib) is the only treatment approved specifically to address PIK3CA mutation
- The approval was based on SOLAR-1 Phase III trial showing Piqray plus fulvestrant nearly doubled median PFS (11.0 vs. 5.7 months) in HR+/HER2- advanced breast cancer patients with PIK3CA mutation, compared to fulvestrant alone.
- Approximately 30-40% of those with HR+/HER2- subtype have a PIK3CA mutation, which is associated with a poor prognosis. In Singapore, the incidence of point mutations in PIK3CA, are amongst the most frequently reported to date for any gene in breast cancer.

Singapore, March 1 , 2021 – Novartis announced the Health Sciences Authority (HSA) has approved* Piqray®, an α-specific class I phosphatidylinositol-3-kinase (PIK3CA) inhibitor, for the treatment of postmenopausal women, and men, with hormone receptor positive (HR+), human epidermal growth factor receptor 2 (HER2-) negative, advanced breast cancer with a PIK3CA mutation in combination with fulvestrant after disease progression following an endocrine-based regimen.[1]

“Novartis has been researching the role of the PIK3CA mutation for more than 20 years and studying how to target this mutation in order to delay disease progression,” said Itsaraet Gosriwatana, Oncology General Manager, Novartis (Singapore). “The understanding of the PIK3CA status is crucial in equipping doctors to develop a better personalized treatment plan for patients. Today, we are pleased to be able to offer patients in Singapore with PIQRAY, an important new therapy for HR+/HER2- advanced breast cancer patients whose tumours have a PIK3CA mutation.”

HSA approval is based on results of the Phase III trial, SOLAR-1, that showed Piqray plus fulvestrant nearly doubled median progression-free survival (PFS) compared to fulvestrant alone in HR+/HER2- advanced breast cancer patients with a PIK3CA mutation (median PFS 11.0 months vs 5.7 months; Hazard Ratio (HR)=0.65, 95% CI: 0.50-0.85; p<0.001).[2] Piqray provided consistent PFS results across pre-specified subgroups, including among patients previously treated with a CDK4/6 inhibitor.[2]

The overall response rate (ORR), an indicator of the proportion of patients who experience at least a 30% reduction in overall tumor size (in patients with measurable disease), was more than doubled when Piqray was added to fulvestrant in patients with a PIK3CA mutation, (ORR = 35.7% vs 16.2% for fulvestrant alone, p=0.0002).[2,3]

Patients with HR+/HER2- advanced breast cancer should be selected for treatment with Piqray, based on the presence of a PIK3CA mutation in tumor tissue or plasma specimens, using a validated test. If a mutation is not detected in a plasma specimen, tumor tissue should be tested if available.[1]

“The PIK3CA gene is frequently mutated in HR+/HER2- breast cancer, affecting about 30% to 40% of people with that subtype 2. Advanced breast cancer patients with the PIK3CA mutations tend to have worse prognosis, developing resistance to standard treatment options more quickly.[6,8,9,10]” said Associate Prof Yap Yoon Sim, Senior Consultant, Division of Medical Oncology, National Cancer Centre Singapore.

In Singapore, a total of 9,634 new cases of breast cancer cases were diagnosed betweeen 2011 – 2015, accounting for nearly 1 in 3 incident cancers in females and making it the most common cancer diagnosis among women. Of which, 1 in 10 women diagnosed with breast cancer are of advanced stages.[7] The incidence of point mutations in PIK3CA, are amongst the most frequently reported to date for any gene in breast cancer in Singapore.[4]

Apprximately 30-40% of those with HR+/HER2- subtype of breast cancer have a PIK3CA mutation[2]. PIK3CA mutations are associated with tumor growth, resistance to endocrine treatment and a poor overall prognosis.[6,8,9,10] Piqray targets the effect of PIK3CA mutations and may help overcome endocrine resistance in HR+ advanced breast cancer.

PIQRAY is the first drug of its kind approved for treatment of postmenopausal women, and men, with hormone receptor positive, HER2- negative, advanced breast cancer with a PIK3CA mutation in Singapore, the European Union,and the United States.

About Piqray® (alpelisib)

Piqray is a kinase inhibitor approved in combination with fulvestrant for the treatment of postmenopausal women, and men, with HR+/HER2-, PIK3CA-mutated, advanced or metastatic breast cancer, as detected by an FDA-approved test following progression on or after endocrine-based regimen.[1]

Approximately 30-40% of HR+ advanced breast cancer patients have a mutation that may activate the PI3K-alpha isoform, called PIK3CA mutations.[2] These mutations are associated with resistance to endocrine therapy, disease progression and a poor prognosis.[6,8,9,10] Piqray works by inhibiting the PI3K pathway, predominantly the PI3K-alpha isoform, to address the effect of PIK3CA mutations.

About SOLAR-1

SOLAR-1 is a global, Phase III randomized, double-blind, placebo-controlled trial studying Piqray in combination with fulvestrant for postmenopausal women, and men, with PIK3CA-mutated HR+/HER2- advanced or metastatic breast cancer that progressed on or following aromatase inhibitor treatment with or without a CDK4/6 inhibitor[2,3]. SOLAR-1 is the pivotal Phase III trial that supported this approval.

The trial randomized 572 patients. Patients were allocated based on central tumor tissue assessment to either a PIK3CA-mutated cohort (n=341) or a PIK3CA non-mutated cohort (n=231). Within each cohort, patients were randomized in a 1:1 ratio to receive continuous oral treatment with Piqray (300 mg once daily) plus fulvestrant (500 mg every 28 days + Cycle 1 Day 15) or placebo plus fulvestrant. Stratification was based on visceral metastases and prior CDK4/6 inhibitor treatment[2,3]. Patients and investigators are blinded to PIK3CA mutation status and treatment. The primary endpoint is local investigator assessed PFS using RECIST 1.1 for patients with a PIK3CA mutation. The key secondary endpoint is overall survival, and additional secondary endpoints include, but are not limited to, overall response rate, clinical benefit rate, health-related quality of life, efficacy in PIK3CA non-mutated cohort, safety and tolerability[2]. SOLAR-1 is ongoing to assess overall survival and other secondary endpoints.

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.

Indication[1]

Piqray is an α-specific class I phosphatidylinositol-3-kinase (PIK3CA) inhibitor indicated for the treatment of postmenopausal women, and men, with hormone receptor positive, HER2- negative, advanced breast cancer with a PIK3CA mutation in combination with fulvestrant after disease progression following an endocrine-based regimen.

Important Safety Information[1]

Treatment with Piqray should be initiated by a physician experienced in the use of anticancer therapies.

Piqray is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients. PIQRAY may cause serious side effects. PIQRAY can cause hypersensitivity (including anaphylactic reaction), manifested by symptoms including, but not limited to, dyspnea, flushing, rash, fever or tachycardia

The most common adverse drug reactions in Piqray plus fulvestrant treated patients were hyperglycaemia, diarrhea, rash, nausea, fatigue and asthenia, decreased appetite, stomatitis, vomiting and weight decreased.

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.

For more information, please see full Prescribing Information for Piqray, available at https://www.novartis.com.sg/product-list/PIQRAY

About Novartis Global

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**HSA approval for PIQRAY on 25th March 2020*

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References

1. Piqray (alpelisib) Singapore Prescribing Information. Novartis Singapore; Jan 2020.
2. André F, Ciruelos E, Rubovszky G. Alpelisib for PIK3CA-Mutated, Hormone-Receptor-Positive Advanced Breast Cancer. N Eng J Med 2019.
3. Juric D, Ciruelos EM, Rubovszky G et al. Alpelisib (ALP) + fulvestrant (FUL) for advanced breast cancer (ABC): Phase 3 SOLAR-1 trial results. Presented at the San Antonio Breast Cancer Symposium (SABCS) (Abstract #GS3-08) on December 6, 2018.
4. Liang, X., Lau, Q., Salto-Tellez, M., Putti, T., Loh, M. and Sukumar, S., 2006. Mutational hotspot in Exon 20 of PIK3CA in breast cancer among singapore chinese. Cancer Biology & Therapy, 5(5), pp.544-548.
5. Moynahan ME, Chen D, He W, et al. Br J Cancer. 2017;116(6):726-730002E
6. Miller TW, Rexer BN, Garrett JT, et al. Mutations in the Phosphatidylinositol 3-Kinase Pathway: Role in Tumor Progression and Therapeutic Implications in Breast Cancer. Breast Cancer Res. 2011.
7. National Registry of Diseases Office (NRDO).Singapore Cancer Registry Annual Registry Report 2015. Jun 2017
8. Sobhani N, Roviello G, Corona SP et al. The prognostic value of PI3K mutational status in breast cancer: a meta-analysis. J Cell Biochem. 2018;119(6):4287-4292.
9. Sabine V, Crozier C, Brookes C, et al. Mutational analysis of PI3K/AKT signaling pathway in tamoxifen exemestane adjuvant multinational pathology study. Journal of Clinical Oncology. 2014;32:2951-2958.
10. Saal LH, Johansson P, Holm K. Poor prognosis in carcinoma is associated with a gene expression signature of aberrant PTEN tumor suppressor pathway activity. PNAS. 2007;104(18):7564-7569.

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