## Piqray® (alpelisib) – New drug approval

- On May 24, 2019, the FDA announced the approval of Novartis' Piqray (alpelisib) in combination with Faslodex® (fulvestrant) for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.
    - The FDA also approved Qiagen's companion diagnostic test, therascreen® PIK3CA RGQ PCR Kit, to detect the PIK3CA mutation in a tissue and/or a liquid biopsy.
    - Piqray is the first new drug application for a new molecular entity approved under the Real-Time Oncology Review pilot program, which permits the FDA to begin analyzing key efficacy and safety datasets prior to the official submission of an application, allowing the review team to begin their review and communicate with the applicant earlier.
- PIK3CA is the most commonly mutated gene in HR+/HER2- breast cancer; approximately 40% of patients living with HR+/HER2- breast cancer have this mutation. PIK3CA mutations are associated with tumor growth, resistance to endocrine treatment and a poor overall prognosis.
- Piqray is a kinase inhibitor that targets the effects of PIK3CA mutations.
- The efficacy of Piqray was studied in the SOLAR-1 clinical trial of 572 postmenopausal women and men with HR-positive, HER2-negative, advanced or metastatic breast cancer whose cancer had progressed while on or after receiving an aromatase inhibitor. Patients received either Piqray or placebo, plus Faslodex. The major efficacy outcome was progression free survival (PFS). Other outcome measures included overall response rate (ORR) and overall survival (OS).
    - The addition of Piqray to Faslodex significantly prolonged PFS (median of 11 months vs. 5.7 months) in patients whose tumors had a PIK3CA mutation (HR = 0.65; 95% CI 0.50, 0.85; p = 0.0013).
    - No PFS benefit was observed in patients whose tumors did not have a PIK3CA tissue mutation (HR = 0.85; 95% CI: 0.58, 1.25).
    - The ORR was greater in the Piqray plus Faslodex group vs. the placebo plus Faslodex group [35.7% (95% CI: 27.4, 44.7) vs. 16.2% (95% CI: 10.4, 23.5)].
    - At the time of final PFS analysis, 27% (92/341) of patients had died, and OS follow-up was immature.
- Warnings and precautions of Piqray include severe hypersensitivity, severe cutaneous reactions, hyperglycemia, pneumonitis, diarrhea, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) reported with Piqray use were increased glucose, increased creatinine, diarrhea, rash, decreased lymphocyte count, increased gamma glutamyl transferase, nausea, increased alanine aminotransferase, fatigue, decreased hemoglobin, increased lipase, decreased appetite, stomatitis, vomiting, decreased weight, decreased calcium, decreased glucose, prolonged activated partial thromboplastin time, and alopecia.
- The recommended dose of Piqray is 300 mg (two 150 mg tablets) taken orally, once daily, with food. Treatment is continued until disease progression or unacceptable toxicity.
    - When given with Piqray, the recommended dose of Faslodex is 500 mg administered intramuscularly on days 1, 15, and 29 and once monthly thereafter. Refer to the Faslodex drug label for further dosing information.

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- Novartis plans to launch Piqray on May 29, 2019. Piqray will be available as 50 mg, 150 mg and 200 mg tablets.