Itovebi™ (inavolisib) – New drug approval

- On October 10, 2024, the FDA announced the approval of Genentech's Itovebi (inavolisib), in combination with Ibrance® (palbociclib) and fulvestrant, for the treatment of adults with endocrine-resistant, PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy.

- HR-positive breast cancer accounts for approximately 70% of all breast cancer cases.

    — The PIK3CA mutation is found in approximately 40% of HR-positive metastatic breast cancers.

- Itovebi is a phosphatidylinositol 3-kinase (PI3K) inhibitor.

- The efficacy of Itovebi was established in INAVO120, a randomized, double-blind, placebo-controlled study in adult patients with endocrine-resistant PIK3CA-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer whose disease progressed during or within 12 months of completing adjuvant endocrine therapy and who have not received prior systemic therapy for locally advanced or metastatic disease. Patients received either Itovebi or placebo, in combination with Ibrance plus fulvestrant. The major efficacy outcome measure was progression-free survival (PFS). Additional outcome measures included overall survival (OS), objective response rate (ORR), and duration of response (DOR).

    — Median PFS was 15.0 months in the Itovebi arm vs. 7.3 months in the placebo arm (hazard ratio 0.43, 95% CI: 0.32, 0.59; $p < 0.0001$).
    — The ORR was 58% (95% CI: 50, 66) in the Itovebi arm vs. 25% (95% CI: 19, 32) in the placebo arm.
    — The median DOR was 18.4 months (95% CI: 10.4, 22.2) in the Itovebi arm vs. 9.6 months (95% CI: 7.4, 16.6) in the placebo arm.
    — At the time of the PFS analysis, OS data were not mature with 30% deaths in the overall population.

- Warnings and precautions for Itovebi include hyperglycemia, stomatitis, diarrhea, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%), including laboratory abnormalities, with Itovebi use were decreased neutrophils, decreased hemoglobin, increased fasting glucose, decreased platelets, decreased lymphocytes, stomatitis, diarrhea, decreased calcium, fatigue, decreased potassium, increased creatinine, increased ALT, nausea, decreased sodium, decreased magnesium, rash, decreased appetite, COVID-19 infection, and headache.

- The recommended dose of Itovebi is 9 mg taken orally once daily, with or without food, until disease progression or unacceptable toxicity.

    — Itovebi should be administered in combination with Ibrance and fulvestrant. The recommended dosage of Ibrance is 125 mg taken orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a cycle of 28 days. Refer to the drug labels for Ibrance and fulvestrant for full dosing information.
    — Patients should be selected for treatment with Itovebi based on the presence of one or more PIK3CA mutations in plasma specimens. Information on FDA-approved tests for the

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detection of PIK3CA mutations in breast cancer is available at: http://www.fda.gov/companiondiagnostics.

- Genentech plans to launch Itovebi in the coming weeks. Itovebi will be available as a 3 mg and 9 mg tablet.