Tukysa™ (tucatinib) – New orphan drug approval

- On April 17, 2020, the FDA announced the approval of Seattle Genetics' Tukysa (tucatinib), in combination with trastuzumab and capecitabine, for treatment of adult patients with advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.

- Patients with HER2-positive breast cancer have tumors with high levels of HER2, which promotes the growth of cancer cells.

    — In the U.S., 279,100 new cases of breast cancer will be diagnosed in 2020. Approximately one-fifth of breast cancers are HER2-positive, and more than 25% of women with metastatic HER2-positive breast cancer will develop brain metastases.

- Tukysa is a HER2 inhibitor. It is designed to inhibit the HER2 protein, which results in the inhibition of cell growth of HER2-expressing tumor cells.

- The efficacy of Tukysa was established in a double-blind, placebo-controlled study in 612 patients who had HER2-positive advanced unresectable or metastatic breast cancer and had prior treatment with trastuzumab, Perjeta® (pertuzumab), and Kadcyla® (ado-trastuzumab emtansine). All patients received baseline trastuzumab and capecitabine and were randomized to receive either Tukysa 300 mg or placebo orally twice daily. The primary endpoint was progression-free survival (PFS). Key secondary endpoints included overall survival (OS) and PFS in patients with brain metastases at baseline.

    — Median PFS was 7.8 months in the Tukysa arm vs. 5.6 months in the control arm (hazard ratio [HR] 0.54; 95% CI: 0.42, 0.71; $p < 0.00001$).
    — Median OS was 21.9 months in the Tukysa arm vs. 17.4 months in the control arm (HR 0.66; 95% CI: 0.50, 0.87; $p = 0.0048$).
    — For patients with brain metastases, median PFS was 7.6 months in the Tukysa arm vs. 5.4 months in the control arm (HR 0.48; 95% CI: 0.34, 0.69; $p < 0.00001$).

- Warnings and precautions for Tukysa include diarrhea, hepatotoxicity, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Tukysa use were diarrhea, palmar-plantar erythrodysesthesia, nausea, fatigue, hepatotoxicity, vomiting, stomatitis, decreased appetite, abdominal pain, headache, anemia, and rash.

- The recommended dose of Tukysa is 300 mg taken orally twice daily in combination with trastuzumab and capecitabine until disease progression or unacceptable toxicity.

    — When given in combination with Tukysa, the recommended dosage of capecitabine is 1000 mg/m^2 orally twice daily taken within 30 minutes after a meal. Tukysa and capecitabine can be taken at the same time.
    — Refer to the drug labels for trastuzumab and capecitabine for additional doing information.

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- Seattle Genetics plans to launch Tukysa within a week of approval. Tukysa will be available as 50 mg and 150 mg tablets.