Truqap™ (capivasertib) – New drug approval

- On November 17, 2023, AstraZeneca announced the FDA approval of Truqap (capivasertib), in combination with fulvestrant, for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with one or more *PIK3CA/AKT1/PTEN*-alterations as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.

- In the U.S., more than 290,000 patients are expected to be diagnosed with breast cancer in 2023, with more than 43,000 deaths.

    - HR-positive breast cancer is the most common subtype of breast cancer with more than 65% of tumors considered HR-positive and HER2-low or HER2-negative.
    - Mutations in *PIK3CA*, *AKT1* and alterations in *PTEN,* affect up to 50% of patients with advanced HR-positive breast cancer.

- Truqap is a first-in-class kinase inhibitor of all three AKT isoforms (AKT1/2/3).

- The efficacy of Truqap was established in CAPItello-291, a randomized, double-blind, placebo-controlled study in 708 adult patients with locally advanced or metastatic HR-positive, HER2-negative breast cancer of which 289 patients had tumors with eligible *PIK3CA/AKT1/PTEN*-alterations. Patients were randomized to receive either Truqap or placebo. Fulvestrant was administered to all patients. The major efficacy outcomes were progression-free survival (PFS) in the overall population, and in the population of patients whose tumors have *PIK3CA/AKT1/PTEN*-alterations.

    - A statistically significant difference in PFS was observed in the overall population and the population of patients whose tumors have *PIK3CA/AKT1/PTEN*-alteration. An exploratory analysis of PFS in the 313 (44%) patients whose tumors did not have a *PIK3CA/AKT1/PTEN*-alteration showed a hazard ratio (HR) of 0.79 (95% CI: 0.61, 1.02), indicating that the difference in the overall population was primarily attributed to the results seen in the population of patients whose tumors have *PIK3CA/AKT1/PTEN*-alteration.
    - In patients with *PIK3CA/AKT1/PTEN*-altered tumors, median PFS was 7.3 months (95% CI: 5.5, 9.0) with Truqap plus fulvestrant vs. 3.1 months (95% CI: 2.0, 3.7) with placebo plus fulvestrant (HR 0.50, 95% CI: 0.38, 0.65; $p < 0.0001$). The ORR was 26% (95% CI: 19, 34) and 8% (95% CI: 4,14), respectively.

- Warnings and precautions for Truqap include hyperglycemia; diarrhea; cutaneous adverse reactions; and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%), including laboratory abnormalities, with Truqap use were diarrhea, cutaneous adverse reactions, increased random glucose, decreased lymphocytes, decreased hemoglobin, increased fasting glucose, nausea, fatigue, decreased leukocytes, increased triglycerides, decreased neutrophils, increased creatinine, vomiting and stomatitis.

- The recommended dosage of Truqap, in combination with fulvestrant, is 400 mg orally twice daily (approximately 12 hours apart) with or without food, for 4 days followed by 3 days off. Truqap should be continued until disease progression or unacceptable toxicity.

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  - — Patients should be selected based on the presence of one or more of the following genetic alterations in tumor tissue: *PIK3CA/AKT1/PTEN.* Information on FDA-approved tests for the detection of *PIK3CA*, *AKT1*, and *PTEN* alterations is available at: http://www.fda.gov/CompanionDiagnostics.

- AstraZeneca's launch plans for Truqap are pending. Truqap will be available as 160 mg and 200 mg tablets.