Lenvima® (lenvatinib) and Keytruda® (pembrolizumab) – New indication

- On September 17, 2019, the FDA announced the approval of Eisai's Lenvima (lenvatinib), used in combination with Merck's Keytruda (pembrolizumab), for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.
    - This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.
- Lenvima is also approved for differentiated thyroid cancer, renal cell carcinoma, and hepatocellular carcinoma.
- Keytruda is also approved for melanoma, non-small cell lung cancer, small cell lung cancer, head and neck squamous cell cancer, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, urothelial carcinoma, MSI-H cancer, gastric cancer, esophageal cancer, cervical cancer, hepatocellular carcinoma, Merkel cell carcinoma, and renal cell carcinoma.
- The approval of Lenvima and Keytruda for endometrial carcinoma was the first FDA action as part of Project Orbis.
    - Project Orbis is an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among its international partners. Under this project, the FDA, the Australian Therapeutic Goods Administration and Health Canada collaboratively reviewed applications for Lenvima and Keytruda, allowing for simultaneous decisions in all three countries.
    - Collaboration among international regulators may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions, regardless of whether the product has received FDA approval. With a framework for concurrent submission and review of oncology drugs, Project Orbis facilitates a collaborative review to identify any regulatory divergence across review teams.
- Endometrial cancer is a disease in which cancer cells form in the tissues of the inner lining of the uterus (endometrium). Endometrial cancer is the most common cancer of the female genital tract.
- The approval of Lenvima and Keytruda for this new indication was based on a single-arm, open-label, multi-cohort trial in 108 patients with metastatic endometrial carcinoma that had progressed following at least one prior systemic therapy in any setting. Patients were treated with Lenvima in combination with Keytruda until unacceptable toxicity or disease progression. The major efficacy outcome measures were objective response rate (ORR) and duration of response (DOR).
    - The ORR was 38.3% (95% CI: 29, 49).
    - The median DOR was not reached (range: 1.2+ months, 33.1+ months). Of responders, 25 patients (69%) had a duration of response ≥ 6 months.
- The most common adverse reactions (≥ 20%) with Lenvima used in combination with Keytruda for endometrial carcinoma were fatigue, hypertension, musculoskeletal pain, diarrhea, decreased appetite, hypothyroidism, nausea, stomatitis, vomiting, decreased weight, abdominal pain,

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headache, constipation, urinary tract infection, dysphonia, hemorrhagic events, hypomagnesemia, palmar-plantar erythrodysesthesia, dyspnea, cough, and rash.

- The recommended dosage of Lenvima for treatment of endometrial carcinoma is 20 mg orally once daily, in combination with Keytruda 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks, until disease progression, unacceptable toxicity, or for Keytruda, up to 24 months in patients without disease progression.

    — Refer to the Lenvima and Keytruda drug labels for dosing for all their other indications.