U.S., Australia and Canada Simultaneously Approve Combo for Endometrial Cancer

Keytruda plus Lenvima is first approval under Project Orbis collaboration.

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FDA takes first action under new international collaboration with Australia and Canada designed to provide a framework for concurrent review of cancer therapies, approving treatment for patients with endometrial carcinoma

The U.S. Food and Drug Administration is announcing Project Orbis, an initiative of the FDA Oncology Center of Excellence (OCE). 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 (TGA) and Health Canada collaboratively reviewed applications for two oncology drugs, allowing for simultaneous decisions in all three countries.

“We are pleased to be working alongside our Australian and Canadian colleagues to help make potentially life-changing treatments available to patients as quickly as possible while still ensuring the FDA’s high standards of safety and effectiveness,” said Acting FDA Commissioner Ned Sharpless, MD “As Project Orbis expands, we look forward to welcoming additional international partners to collaborate with us in this important initiative as we work to help further serve the global patient community.”

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. This is partly due to different standards of care around the world that also have an impact on the increasingly international conduct of cancer clinical trials, potentially slowing the development of anticancer products. 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.

As part of Project Orbis, in conjunction with decisions by TGA and Health Canada, the FDA today granted accelerated approval to Lenvima (lenvatinib) in combination with Keytruda (pembrolizumab) for the treatment of patients with advanced endometrial carcinoma that is not

microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), and who have disease progression following prior systemic therapy but are not candidates for curative surgery or radiation.

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. Obesity, metabolic syndrome, and certain estrogen promoting medications may increase the risk of endometrial cancer. Symptoms may include unusual vaginal bleeding or pain in the pelvis.

“In addition to the international collaboration with Australia and Canada, this review used the ‘Real-Time Oncology Review’ (RTOR) pilot program, which can streamline the submission of data prior to the completion and submission of the entire clinical application,” said Richard Pazdur, MD, director of the FDA’s Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA’s Center for Drug Evaluation and Research. “RTOR, and its accompanying Assessment Aid, facilitated discussions among the regulatory agencies, expediting the approval in the three countries. These applications were approved three months prior to the FDA goal date.”

Lenvima was initially approved by the FDA in 2015 and Keytruda was initially approved in 2014. Today’s approval of Lenvima in combination with Keytruda was based on the results of a clinical trial of 94 patients with endometrial carcinoma tumors that were not MSI-H or dMMR. Of the 94 patients, 10 patients (10.6% of responders) had a complete response, or disappearance of all lesions on imaging, and 26 patients (27.7% of responders) had a partial response, or shrinkage of lesions by at least 30%, leading to an objective response rate of 38.3%. Of these, 25 patients (69% of responders) have a duration of response of greater than 6 months.

Common side effects for patients in the clinical trial included fatigue, high blood pressure, musculoskeletal pain, diarrhea, decreased appetite, hypothyroidism (underactive thyroid), nausea and stomatitis (inflamed and sore mouth). Additional side effects included vomiting, decreased weight, abdominal pain, headache, constipation, urinary tract infection, dysphonia (voice difficulty), hemorrhagic events (bleeding), hypomagnesemia (low magnesium levels), palmar-plantar erythrodysesthesia (hand foot syndrome), dyspnea (shortness of breath), cough and rash. Health care professionals should inform females of reproductive age and males with a female partner of reproductive potential to use effective contraception during treatment with Lenvima in combination with Keytruda. Women who are pregnant or breastfeeding should not take this combination because it may cause harm to a developing fetus or newborn baby.

Lenvima in combination with Keytruda was granted accelerated approval. This approval commits the sponsor to provide additional data to the FDA. The application also received Priority Review and both Lenvima and Keytruda had received Breakthrough Therapy Designation for this indication. This review was conducted under the Oncology Center of Excellence’s RTOR pilot program and Assessment Aid.

The approval was granted to Eisai Inc. and Merck Sharp & Dohme Corp.

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