FDA Approves Drug that Targets Genetic Driver Rather Than Tumor Type

New drug Vitrakvi targets specific receptor kinase that promotes tumors.

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FDA approves an oncology drug that targets a key genetic driver of cancer, rather than a specific type of tumor

The U.S. Food and Drug Administration today granted accelerated approval to Vitrakvi (larotrectinib), a treatment for adult and pediatric patients whose cancers have a specific genetic feature (biomarker).

This is the second time the agency has approved a cancer treatment based on a common biomarker across different types of tumors rather than the location in the body where the tumor originated. The approval marks a new paradigm in the development of cancer drugs that are "tissue agnostic." It follows the policies that the FDA developed in a guidance document released earlier this year.

Vitrakvi is indicated for the treatment of adult and pediatric patients with solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity and have no satisfactory alternative treatments or that have progressed following treatment.

"Today's approval marks another step in an important shift toward treating cancers based on their tumor genetics rather than their site of origin in the body," said FDA Commissioner Scott Gottlieb, MD. "This new site-agnostic oncology therapy isn't specific to a cancer arising in a particular body organ, such as breast or colon cancer. Its approval reflects advances in the use of biomarkers to guide drug development and the more targeted delivery of medicine. We now have the ability to make sure that the right patients get the right treatment at the right time. This type of drug development program, which enrolled patients with different tumors but a common gene mutation, wouldn't have been possible a decade ago because we knew a lot less about such cancer mutations. Using our breakthrough therapy designation and accelerated approval processes, we support innovation in precision oncology drug development and the evolution of more targeted and effective treatments for cancer patients. This is especially true when it comes

to pediatric cancers. We're committed to continuing to advance a more modern framework of clinical trial designs that support more targeted innovations across disease types based on our growing understanding of the underlying biology of diseases like cancer."

Research has shown that the NTRK genes, which encode for TRK proteins, can become fused to other genes abnormally, resulting in growth signals that support the growth of tumors. NTRK fusions are rare but occur in cancers arising in many sites of the body. Prior to today's approval, there had been no treatment for cancers that frequently express this mutation, like mammary analogue secretory carcinoma, cellular or mixed congenital mesoblastic nephroma and infantile fibrosarcoma.

The efficacy of larotrectinib was studied in three clinical trials that included 55 pediatric and adult patients with solid tumors that had an identified NTRK gene fusion without a resistance mutation and were metastatic or where surgical resection was likely to result in severe morbidity. These patients had no satisfactory alternative treatments or had cancer that progressed following treatment.

Larotrectinib demonstrated a 75 percent overall response rate across different types of solid tumors. These responses were durable, with 73 percent of responses lasting at least six months, and 39 percent lasting a year or more at the time results were analyzed. Examples of tumor types with an NTRK fusion that responded to larotrectinib include soft tissue sarcoma, salivary gland cancer, infantile fibrosarcoma, thyroid cancer and lung cancer.

Vitrakvi received an accelerated approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need using clinical trial data that is thought to predict a clinical benefit to patients. Further clinical trials are required to confirm Vitrakvi's clinical benefit and the sponsor is conducting or plans to conduct these studies.

Common side effects reported by patients receiving Vitrakvi in clinical trials include fatigue, nausea, cough, constipation, diarrhea, dizziness, vomiting, and increased AST and ALT enzyme blood levels in the liver. Health care providers are advised to monitor patient ALT and AST liver tests every two weeks during the first month of treatment, then monthly and as clinically indicated. Women who are pregnant or breastfeeding should not take Vitrakvi because it may cause harm to a developing fetus or newborn baby. Patients should report signs of neurologic reactions such as dizziness.

The FDA granted this application Priority Review and Breakthrough Therapydesignation. Vitrakvi also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted the approval of Vitrakvi to Loxo Oncology.

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