FDA approves the first targeted therapy to treat a rare mutation in patients with gastrointestinal stromal tumors
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The U.S. Food and Drug Administration approved Ayvakit (avapritinib) for the treatment of adults with unresectable (unable to be removed with surgery) or metastatic (when cancer cells spread to other parts of the body) gastrointestinal stromal tumor (GIST) - a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine - harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation. This approval includes GIST that harbors a PDGFRA D842V mutation, which is the most common exon 18 mutation. Ayvakit is a kinase inhibitor, meaning it blocks a type of enzyme called a kinase and helps keeps the cancer cells from growing.

"GIST harboring a PDGFRA exon 18 mutation do not respond to standard therapies for GIST. However, today's approval provides patients with the first drug specifically approved for GIST harboring this mutation," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "Clinical trials showed a high response rate with almost 85% of patients experiencing tumor shrinkage with this targeted drug."

GISTs arise from specialized nerve cells found in the walls of the gastrointestinal tract. One or more mutations in the DNA of one of these cells may lead to the development of GIST. These cells aid in the movement of food through the intestines and control various digestive processes. More than half of GISTs start in the stomach. Most of the others start in the small intestine, but GISTs can start anywhere along the gastrointestinal tract. The activating mutations in PDGFRA have been linked to the development of GISTs, and up to approximately 10% of GIST cases involve mutations of this gene.

The FDA approved Ayvakit based on the results of a clinical trial involving 43 patients with GIST harboring a PDGFRA exon 18 mutation, including 38 patients with PDGFRA D842V mutation. Patients received Ayvakit 300 mg or 400 mg orally once daily until disease progression or they experienced unacceptable toxicity. The recommended dose was determined to be 300 mg once daily. The trial measured how many patients experienced complete or partial shrinkage (by a certain amount) of their tumors during treatment (overall response rate). For patients harboring a PDGFRA exon 18 mutation, the overall response rate was 84%, with 7% having a complete response and 77% having a partial response. For the subgroup of patients with PDGFRA D842V mutations, the overall response rate was 89%, with 8% having a complete response and 82% having a partial response. While the median duration of response was not reached, 61% of the responding patients with exon 18 mutations had a response lasting six months or longer (31% of patients with an ongoing response were followed for less than six months).

Common side effects for patients taking Ayvakit were edema (swelling), nausea, fatigue/asthenia (abnormal physical weakness or lack of energy), cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation (secretion of tears), abdominal pain, constipation, rash and dizziness. Ayvakit can cause intracranial hemorrhage (bleeding that occurs inside the skull) in which case the dose should be reduced, or the drug should be discontinued. Ayvakit can also cause central nervous system effects including cognitive impairment, dizziness, sleep disorders, mood disorders, speech disorders and hallucinations. If this happens, depending on the severity, Ayvakit should be withheld

and then resumed at the same or reduced dose upon improvement or permanently discontinued.

Health care professionals should advise pregnant women that Ayvakit may cause harm to a developing fetus or newborn baby. Additionally, the FDA advises health care professionals to tell females of reproductive potential, and males with female partners of reproductive potential, to use effective contraception during treatment with Ayvakit and for six weeks after the final dose.

The FDA granted this application Breakthrough Therapy designation, which expedites the development and review of drugs that are intended to treat a serious condition, when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. Ayvakit was also granted Fast Track designation, which expedites the review of drugs to treat serious conditions and fill an unmet medical need. Ayvakit received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted approval of Ayvakit to Blueprint Medicines Corporation.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.