Ivosidenib earns FDA approval against IDH1+ acute myeloid leukemia

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Daniel A. Pollyea, MD, MS and colleagues report clinical trial results leading to FDA approval of ivosidenib against IDH1+ AML. Credit: University of Colorado Cancer Center

Clinical trials at University of Colorado Cancer Center and elsewhere now result in the drug ivosidenib earning approval from the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (R/R AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation. Ivosidenib, an oral, targeted inhibitor of the IDH1 enzyme, is the first and only FDA-approved therapy for patients with R/R AML and an IDH1 mutation.

"Ivosidenib is an important new weapon in the arsenal," says Daniel A. Pollyea, MD, MS, investigator at CU Cancer Center, clinical director of Leukemia Services at the CU School of Medicine, and principal investigator of early ivosidenib trials. "It's a very well tolerated oral therapy for patients who have few options and it is an important new tool for us to use."

AML is a cancer of the blood and bone marrow marked by rapid disease progression and is the most common acute leukemia affecting adults with approximately 20,000 new cases estimated in the U.S. each year. The majority of patients with AML eventually relapse. Relapsed or refractory AML has a poor prognosis. The five-year survival rate is approximately 27 percent. For 6 to 10 percent of AML patients, the mutated IDH1 enzyme activates other oncogenes while muting the action of tumor-suppressor genes, contributing to the genesis of the disease. Ivosidenib seeks to disrupt the action of the mutated IDH1 gene.

In results presented by Dr. Pollyea at the American Society of Clinical Oncology (ASCO) Annual Meeting 2018, 41.9 percent of 258 patients with IDH1+ AML treated with ivosidenib responded to treatment, with median progression free survival of 8.2 months. Twenty-four percent of patients achieved a complete response.

"This drug showed great promise, even during the earliest clinical trial. Many of the patients we treated here have derived great benefit and we are excited to have had the opportunity to treat so many patients from our region with this exciting and effective therapy years before it was approved for general use by the FDA," says Pollyea.

The drug, developed by Agios Pharmaceuticals Inc., is similar in design and action to the drug enasidenib, which targets the related gene IDH2, and which earned FDA approval in 2017.

"We know about 50 or so genes that contribute to AML and now researchers are working to design and test drugs that treat the most common and the most powerful of these genes," Pollyea says.

The approval of ivosidenib makes available for clinical practice the first targeted therapy for adult patients with relapsed/refractory acute myeloid leukemia and an IDH1 mutation.

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