FDA Approves Revuforj, the First Menin Inhibitor, for Acute Leukemia [UPDATED]

About 1 in 5 patients treated with revumenib achieved complete remission, and some were able to receive a curative stem cell transplant.

December 10, 2024 By Liz Highleyman

On November 15, the Food and Drug Administration (FDA) approved Revuforj (revumenib), a first-in-class menin inhibitor, for the treatment of adults and children with relapsed or refractory acute leukemia with a KMT2A gene translocation.

Revuforj, from Syndax Pharmaceuticals, interferes with the interaction between menin, a scaffold protein, and histone-lysine N-methyltransferase 2A, a protein encoded by the KMT2A gene. KMT2A gene alterations can trigger production of leukemia cells, and people with these mutations tend to have aggressive disease. Menin inhibitors bind to menin and halt this process, returning to production of normal cells.

"The FDA approval of the first menin inhibitor is a major breakthrough for patients with relapsed or refractory acute leukemia with a KMT2A translocation, a genetic alteration associated with a very poor prognosis," Ghayas Issa, MD, a leukemia specialist at the University of Texas MD Anderson Cancer Center, said in a news release. "The significant clinical benefit and robust efficacy seen with Revuforj represents a substantial improvement over what has been historically observed in these patients with previously available therapies and has the potential to be an important new treatment option for patients."

The approval is supported by results from the Phase I/II AUGMENT-101 trial (NCT04065399), which evaluated Revuforj in people with relapsed or refractory (nonresponsive) acute leukemia. The study included 104 adult and pediatric patients with a KMT2A gene translocation, most of whom had tried multiple prior therapies. Acute myeloid leukemia (AML) was the most common diagnosis among adults, while more children had acute lymphoblastic or lymphocytic leukemia (ALL). They received Revuforj tablets twice daily until they experienced disease progression or unacceptable side effects, did not achieve a leukemia-free state after four cycles of treatment or underwent stem cell transplantation.

As reported at last year's American Society of Hematology annual meeting and in the Journal of

Clinical Oncology, Revuforj led to complete or partial remission in nearly two thirds of study participants. Among the 22 patients (21%) with KMT2A translocations who achieved complete remission or complete remission with partial hematologic recovery (CR+CRh), the median duration of remission was 6.4 months. The CR+CRh rate was comparable for adults and children. Among the 83 people who required red blood cell or platelet transfusions at baseline, 14% became transfusion independent for at least 56 days. In some cases, treatment with Revuforj enabled patients to receive a curative stem cell transplant.

Revuforj was generally safe, and side effects were described as "manageable." The most common adverse reactions include hemorrhage, nausea, diarrhea, constipation, decreased appetite, fatigue, musculoskeletal pain, swelling, infections, febrile neutropenia (fever with low neutrophil count), elevated liver enzymes and other laboratory abnormalities. The prescribing information includes warnings about differentiation syndrome (a rapid release of cytokines as cells return to normal) and QTc prolongation (a reversible heart rhythm abnormality).

Revuforj is also being evaluated for the treatment of acute myeloid leukemia with a different mutation (mNPM1), and multiple trials of Revuforj in combination regimens are ongoing, including some for newly diagnosed patients.

[Update 12/11/24: Researchers presented further data at the American Society of Hematology annual meeting. In a larger data set from the AUGMENT-101 cohort with KMT2A translocations, responses were observed across all major subgroups, including patients of all ages, heavily treatment-experienced patients and those who had previously used Venclexta (venetoclax). Data were also presented from the trial's mNPM1 cohort. In this group of 64 AML patients, the CR+CRh rate was 23%. Among these responders, the median duration of response was 4.7 months at the time of the data cutoff, with three people remaining in remission. Nearly two thirds of those assessed for minimal residual disease (MRD) status were MRD negative. Here too, responses were observed across subgroups, including patients with multiple prior lines of treatment. The CR+CRh rate was 44% for patients who had not previously used Venclexta, falling to 17% for those who had. Historically, AML patients are unlikely to respond to subsequent therapy after Venclexta fails, according to a Syndax news release.]

The 110 mg and 160 mg Revuforj tablets should now be available through a network of specialty distributors and specialty pharmacies, at a cost of around $39,500 per month. However, the 25 mg tablets—which are used to treat people weighing less than 88 pounds—will not be commercially available until the late first quarter or early second quarter of 2025; until then, an oral solution will be available through an expanded access program, according to Syndax.

In a January 2023 article about trends in blood cancer, Leukemia and Lymphoma Society chief scientific officer Lee Greenberger, PhD, predicted that menin inhibitors "could be the next new class of drug approved to treat some forms of acute myeloid leukemia," potentially available in two to five years. With Revuforj, the speed of approval exceeded his expectations.

Click here for full prescribing information for Revuforj.

Click here for more news about blood cancer.
