Break Through Cancer Announces First Patient Enrolled in Phase 2 Trial Targeting Residual Disease in AML

The novel study explores the effects of menin inhibition in acute myeloid leukemia with minimal residual disease as an endpoint.

CAMBRIDGE, MA, UNITED STATES, November 1, 2024 /EINPresswire.com/ -- Break Through Cancer, a Boston-based cancer research foundation, has launched a clinical trial to explore if an investigational drug can eliminate minimal residual disease (MRD) in acute myeloid leukemia (AML).

AML often responds well to initial treatment, but residual cancer cells frequently cause relapse. Break Through Cancer's Eradicating Minimal Residual Disease in AML TeamLab aims to accelerate cures by understanding and targeting MRD in AML, a cancer with a five-year survival rate of 30% for adults.

The TeamLab has enrolled the first patient in a phase 2 clinical trial (NCT06284486) studying whether revumenib and venetoclax in combination clears MRD in AML, and if clearance correlates with longer, progression-free survival. It's among the first trials to use MRD as an endpoint.

"We're hoping by targeting MRD that we're going to prevent relapse in these patients, and hopefully, they will have longer remissions without leukemia," says Ghayas Issa, MD, medical oncologist in the Departments of Leukemia and Genomic Medicine at The University of Texas MD Anderson Cancer Center, Houston, TX, and TeamLab member.

Break Through Cancer's "radical collaboration" model enables real-time data and discovery sharing across top U.S. cancer research centers: MD Anderson, Dana-Farber Cancer Institute, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, MIT's Koch Institute for Integrative Cancer Research, and Memorial Sloan Kettering Cancer Center.

MD Anderson is the first center to enroll patients, and the trial will soon activate across other Break Through Cancer clinical sites. "It's a large collaborative effort," adds Issa. "The protocol and every step of this has been done in collaboration with teammates at each of the institutions."

Intercepting relapse

The trial will assess safety and tolerability of a two-drug combination. The first is revumenib, an investigational small molecule drug developed and provided by Syndax Pharmaceuticals, which targets menin, a protein involved in cancer progression in select AML patients with particular mutations (NPM1, NUP98, or KMT2A).

In earlier phase 1 and phase 2 trials, Issa and colleagues demonstrated the safety and efficacy of revumenib in certain AML patients with KMT2A or NPM1 mutations. Treatment led to complete remission in about 30% of patients. “Revumenib is promising, and we hope it will become standard-of-care for patients with these mutations who need it,” says Issa.

The second drug is venetoclax, an approved drug made by AbbVie, which blocks BCL2 activity, priming cells for a form of cell death. Research suggests that inhibition of menin (revumenib) and BCL2 (venetoclax) in combination could eradicate leukemia better than menin inhibition alone.

“There is a really strong rationale for using these two drugs,” says Jacqueline Garcia, MD, medical oncologist in the Adult Leukemia Program at Dana-Farber Cancer Institute in Boston, MA, and TeamLab member. “If we can more deeply clear the leukemia, we will be more likely to get rid of residual cells that have additional mutations present.”

Researchers will assess MRD clearance and whether it correlates with longer, progression-free survival. Additionally, the team will analyze patient samples to better understand MRD, like whether there are biomarkers to predict drug response, new ways to measure low levels of MRD, and optimal MRD sampling times.

“We’re trying to develop better tools to detect measurable residual disease from a quantitative and qualitative perspective,” says Garcia. “What’s leftover, and what does it mean, and when do we actually do something about it?”

This information could help determine how and when to target residual cancer cells before the cancer can progress. Early intervention, before recurrence, could possibly cure AML.

Further information about the Eradicating Minimal Residual Disease in AML is at https://breakthroughcancer.org/projects/eradicating-minimal-residual-disease-in-aml/.

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About the trial

Title: A Multi-Site Break Through Cancer Trial: Phase II Study Investigating Dual Inhibition of BCL2 and Menin in AML MRD Using the Combination of Venetoclax and Revumenib (NCT06284486)

About Break Through Cancer

Founded in 2021, Break Through Cancer empowers outstanding researchers and physicians to both intercept and find cures for several of the deadliest cancers by stimulating radical collaboration among outstanding cancer research institutions, including its founding partners: Dana-Farber Cancer Institute, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Memorial Sloan Kettering Cancer Center, MIT's Koch Institute for Integrative Cancer Research, and The University of Texas MD Anderson Cancer Center.

The Foundation is supported by a Board of Directors from the five partner institutions and a Scientific Advisory Board of U.S. cancer experts. The Foundation was launched with an extraordinary challenge pledge of $250 million from Mr. and Mrs. William H. Goodwin, Jr. and their family, and the estate of William Hunter Goodwin III.

For further information, please visit the Foundation's website at www.breakthroughcancer.org.

About Revumenib

Revumenib is an oral, small molecule inhibitor of the menin-KMT2A binding interaction being developed for the treatment of KMT2A-rearranged (KMT2Ar) acute leukemias including acute lymphoid leukemia (ALL) and AML, and mutant nucleophosmin (mNPM1) AML. A New Drug Application for revumenib in relapsed/refractory (R/R) KMT2Ar acute leukemia is under Real-time Oncology Review by the U.S. FDA with a PDUFA action date of December 26, 2024. Revumenib was granted Orphan Drug Designation for the treatment of AML and ALL by the FDA and the treatment of AML by the European Commission, and Fast Track designation by the FDA for the treatment of R/R acute leukemias harboring a KMT2A rearrangement or NPM1 mutation. Revumenib was granted Breakthrough Therapy Designation by the FDA for the treatment of R/R acute leukemia harboring a KMT2A rearrangement.

About VENCLEXTA® (venetoclax tablets) (US)

VENCLEXTA® is a first-in-class medicine that selectively binds and inhibits the B-cell lymphoma-2 (BCL-2) protein. In some blood cancers, BCL-2 prevents cancer cells from undergoing their natural death or self-destruction process, called apoptosis. VENCLEXTA targets the BCL-2 protein and works to help restore the process of apoptosis.1 VENCLEXTA is jointly commercialized by AbbVie and Genentech, a member of the Roche Group, in the U.S. and by AbbVie outside of the U.S. Together, the companies are committed to BCL-2 research and to studying venetoclax in clinical trials across several blood cancers.

Ref:
1. VENCLEXTA (venetoclax) [Package Insert]. North Chicago, Ill.: AbbVie

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