Landscape for acute myeloid leukemia patients evolving rapidly as research discoveries advance new treatments

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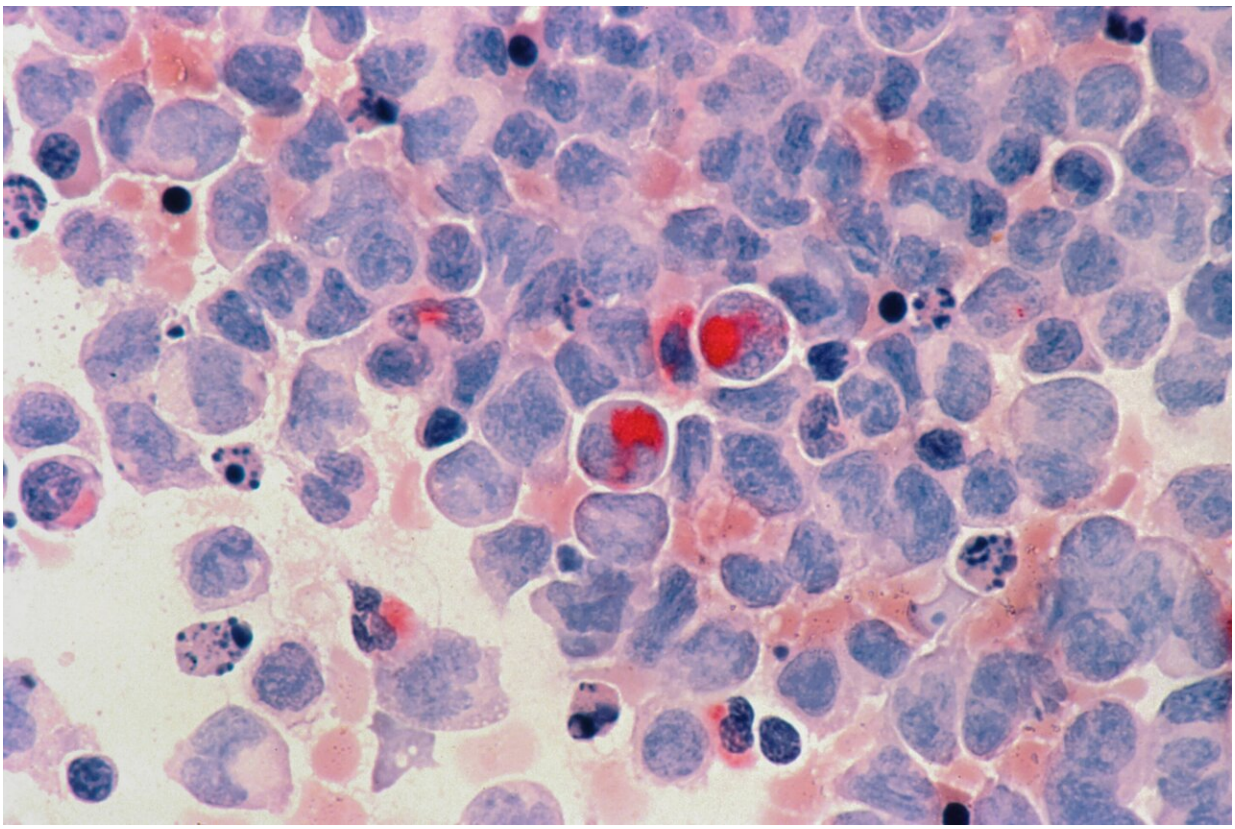

Acute myelocytic leukemia (AML). Credit: Unsplash/CC0 Public Domain

The treatment landscape for acute myeloid leukemia (AML) is evolving rapidly, as research discoveries at Sylvester Comprehensive Cancer

Center at the University of Miami Miller School of Medicine and other academic cancer centers advance new, more effective therapies for this aggressive blood cancer.

"We've seen more progress during the past 10 years than the previous four decades combined," said Justin M. Watts, M.D., Sylvester hematologist, associate professor of medicine, and Pap Corps Early Career Endowed Professor in Leukemia, "especially when it comes to treating older AML patients."

Watts, who serves as chief of the leukemia section at Sylvester, will highlight new drugs, such as Venetoclax plus Azacitidine, and new targeted therapies resulting from research advances when he leads an educational session at ASH 2023, the annual meeting of the American Society of Hematology in San Diego, held Dec. 9–12.

The session is designed to update community-based physicians who treat AML patients on current standards of care for using these new drugs sequentially or in triplet combinations with targeted inhibitors.

Background

Acute myeloid leukemia is a cancer characterized by the rapid growth of abnormal cells that build up in the bone marrow and blood and interfere with normal blood-cell production. It's one of the most common leukemia types in adults, although it's fairly rare, accounting for about 1% of all cancers.

It tends to afflict older adults, with 68 being the median age when first diagnosed, according to the American Cancer Society. Men are slightly more at risk than women.

Typically, AML patients have been treated with intensive chemotherapy

and a bone-marrow or stem-cell transplant. Those therapies are generally more effective in people under age 60. "We can cure about 60% of younger patients now, which is significantly better than just two decades ago," said Watts. "But older patients, depending on their fitness level, don't usually tolerate these treatments and historically less than 10 percent were cured, but this is now pushing 30% with the advent of venetoclax plus azacitidine and targeted inhibitors."

Until recently, next steps for these patients were limited to supportive care and blood transfusions, he added.

Targeted therapies for mutations

However, the outlook has improved, especially for older patients, with the emergence of new drugs and targeted inhibitors for the mutations driving AML, Watts says.

"AML is almost always driven by mutations acquired over time," he explained. "That's why the risk of AML increases as we age."

Although there are hundreds of mutations that can cause this blood cancer, and most patients have more than one, there are five more common ones that are targetable: IDH1, IDH2, FLT3, NPM1 and MLL, Watts said. All of these now have approved therapies—or ones in development—thanks to ongoing research at Sylvester and other cancer centers.

The results are encouraging. "We're seeing very promising results in our studies and trials, combining Venetoclax, Azacitidine and targeted therapies, often as frontline therapy for AML," he noted.

Watts said the combination of Venetoclax and Azacitidine is producing good outcomes in about 52% of older patients, and the median survival

is more than two years in these patients, with some patients living much longer.

Additionally, targeted therapies are proving effective, even in relapsed patients, and these treatments are also better tolerated than chemotherapy.

Now, researchers like Watts and his colleagues must determine the best way to combine venetoclax and targeted therapies to produce the best outcomes. "That includes designing clinical trials to help us identify the optimal combinations for the right patients with specific mutations," he explained, "and determining when we stop therapy for patients in a long remission."

On the horizon

Watts said that up to 50% of AML patients have a mutation for which there is no current targeted therapy. "We have to expand our targeted therapies to treat AML patients with harder to target mutations," he explained, citing TP53 and RAS mutations as two common pathways for treatment resistance. "We currently have few approved therapies that are effective for these patients, especially if they are older."

Watts believes the future direction for AML treatment will involve targeted therapy combined with the "best backbone we have, possibly chemotherapy for younger patients or the drugs like venetoclax and azacitidine generating good results for older adults."

One of the biggest things that may come into play is immunotherapy, he said. "I can see us getting the immune system more involved in treating these blood cancers, as it has done with solid tumors and lymphoma."

More information: "The Future Paradigm of HMA + VEN or

Targeted Inhibitor Approaches: Sequencing or Triplet Combinations in AML Therapy"

Provided by University of Miami Leonard M. Miller School of Medicine