

[Oncology/Hematology](#) > [Leukemia](#)

Year in Review: Acute Myeloid Leukemia

— Improved survival, individualized treatment, extending transplant to more patients

by [Charles Bankhead](#), Senior Editor, MedPage Today November 29, 2020

Last Updated November 30, 2020



A 10-month survival improvement for older adults with acute myeloid leukemia (AML) earned professional plaudits and [FDA approval](#) for oral azacitidine (Onureg) as maintenance therapy after first remission.

Principal supporting data for the approval came from the phase III [QUAZAR AML-001](#) trial, a placebo-controlled trial involving 472 patients, ages 55 or older, with transplant-ineligible AML in first remission after standard induction therapy. Patients randomized to the active therapy had a median OS of 24.7 months versus 14.8 months for the placebo group. The difference represented a 31% reduction in

CELGENE 2068
APOTEX v. CELGENE
IPR2023-00512

the survival hazard ($P=0.0009$).

"This approval should help establish continued treatment with Onureg as a standard component of AML therapy for adults who achieved first complete remission following chemotherapy and who cannot proceed to intensive curative therapy, like hematopoietic stem-cell transplant," principal investigator Andrew Wei, MD, PhD, of Monash University in Melbourne, Australia, said in a statement from trial sponsor Bristol-Myers Squibb.

In addition to the FDA approval, the QUAZAR results earned oral azacitidine a place in the regional finals of *MedPage Today's* first [OncMadness](#) competition recognizing major developments in the field of oncology. OncMadness panelist David Hermel, MD, of the Scripps Clinic in La Jolla, California, said the trial results have far-reaching implications for management of a disease that typically affects older individuals who have few treatment options.

Following are other highlights of advances in AML management in 2020.

Combination Boosts Survival

Adding the Bcl-2 inhibitor venetoclax (Venclexta) to standard therapy for AML led to statistically significant and clinically meaningful improvement in overall survival (OS), according to a report during the [European Hematology Association virtual meeting](#).

Median OS increased from 9.6 months with standard azacitidine to 14.7 months with the combination. More than twice as many patients achieved complete responses (with or without complete hematologic recovery) with the combination (66.4% vs 28.3%, $P<0.001$). The addition of venetoclax was associated with a 4-month improvement in median duration of response (17.5 vs 13.4 months), and substantially more patients achieved transfusion

independence with combination therapy, whether defined by red cell count (60% vs 35%), platelet count (69% vs 50%), or both (58% vs 34%).

"Responses (with the combination) occurred rapidly, often within one cycle and were seen across all cytogenetic risk groups and molecular mutations," said Courtney DiNardo, MD, of the MD Anderson Cancer Center in Houston. "The safety profile includes increased cytopenias, in particular neutropenia, which can be effectively managed with appropriate neutropenia management guidelines."

The results suggest "a true paradigm shift in the treatment of older patients with AML," she added.

Medical News from Around the Web**STAT**

A breakthrough cystic fibrosis drug gave them the gift of time. But miracles come with complications.

HARVARD HEALTH

When — and how — should you be screened for colon cancer? - Harvard Health

ABC NEWS

Mississippi sees 10-fold increase in babies born with syphilis since 2016: Report

The findings came from the [VIALE-A](#) trial, which involved 431 patients with newly diagnosed AML and who had a median age of 76. They were randomized 2:1 to azacitidine plus venetoclax or placebo. The primary endpoint was OS, and secondary endpoints included complete response, transfusion independence, and event-free survival.

Liposomal Drug Outperforms Standard Therapy

Median OS improved by almost 8 months among patients with AML and myelodysplasia-related changes (AML-MRC) treated with liposomal cytarabine-daunorubicin (CPX-351, Vyxeos) versus conventional 7 + 3 induction therapy, as

reported at the [Transplantation and Cellular Therapy Meetings](#).

Patients treated with CPX-351 had a median OS of 19.15 months as compared with 11.58 months for conventional formulations of cytarabine and daunorubicin. Complete response (CR, including incomplete hematologic recovery, CRi) occurred in 48% of the CPX-351 group versus 33% of patients who received conventional therapy. CPX-351 outperformed standard therapy regardless of prior exposure to hypomethylating agents, and results were similar for patients with AML with or without MRC, reported Stefan Faderl, MD, of Jazz Pharmaceuticals in Hackensack, New Jersey.

The findings came from a subgroup analysis of a phase III trial involving 309 patients with newly diagnosed, high-risk secondary AML, including 246 who met [World Health Organization criteria](#) for AML-MRC. They were randomized 2:1 to CPX-351 or conventional therapy, and the primary endpoint was CR. Among patients who achieved a CR or CRi, CPX-351 led to a 42% reduction in the survival hazard, as well as substantial improvement in 1-year OS (64% vs 43%), 2 year OS (48% vs 31%) and in patients with myelodysplastic syndrome (MDS) karyotype or antecedent MDS.

Guideline Supports Individualized Tx Decisions

Whenever feasible, patients with AML, including appropriately selected and counseled individuals, should receive chemotherapy instead of supportive care and more-intensive versus less-intensive therapy, according to new recommendations from the [American Society of Hematology](#) (ASH).

For patients in end-of-life or hospice care, providers should offer palliative red-cell transfusions, which have proven beneficial in patients not receiving antileukemic therapy.

Regardless of the treatment strategy, careful and thorough discussion between providers and patients should form the basis for clinical decision-making, according to the ASH guideline.

Other recommendations support postremission therapy versus no additional therapy for patients who achieve remission, use of hypomethylating agents or low-dose cytarabine for patients ineligible for intensive therapy, and continued treatment for patients who respond to less-intensive therapy without intolerable side effects.

Antibody May Increase Transplant Eligibility

Four times as many patients qualified for allogeneic stem-cell transplant (SCT) after conditioning therapy with a radiolabeled anti-CD45 antibody versus a standard-of-care conditioning regimen, data from a randomized trial showed.

After conditioning with ^{131}I apamistamab (lomab-B), 31 of 37 patients underwent SCT as compared with seven of 38 patients randomized to standard conditioning therapy. Additionally, 20 patients who did not become transplant eligible with standard therapy crossed over to the antibody, and all 20 subsequently underwent SCT, reported Boglarka Gyurkocza, MD, of Memorial Sloan Kettering Cancer Center in New York City, at the [Transplantation and Cellular Therapy Meetings](#).

Conditioning with the radiolabeled antibody followed by SCT led to neutrophil and platelet engraftment in 100% of patients and no graft failures, she added.

The findings came from a planned interim analysis after 50% enrollment in the phase III [SIERRA](#) trial, involving patients with relapsed/refractory AML. They were randomized to the radiolabeled antibody or standard conditioning therapy. The primary endpoint was durable CR, defined as a CR lasting at least 6 months.

"This is a population who are not generally considered candidates for transplant," said Gyurkocza. "There was a low rate of nonrelapse mortality associated with iomab-B-based conditioning, and the iomab-B-based conditioning regimen had a favorable nonhematologic toxicity profile."

MRD as Trial Endpoint Could Speed New Therapies

Therapies that achieved negative measurable residual disease (MRD) status in clinical trials of AML significantly improved survival, according to a meta-analysis of more than 80 studies involving 11,000 patients.

MRD-negative status was associated with a 63% reduction in the hazard for disease-free survival (95% CI 0.34-0.40) and a 64% reduction in the OS hazard (95% CI 0.33-0.39). The MRD-negative group had an estimated 5-year DFS of 76% versus 25% for the MRD-positive group and estimated 5-year OS of 68% vs 34%, reported Farhad Ravandi, MD, of the MD Anderson Cancer Center in Houston, and colleagues in *JAMA Oncology*.

The association between MRD negativity and survival "was observed across ages, disease subtypes, time of assessment, specimen source, and most MRD detection methods," the authors noted.

"Given the robustness of the association of MRD with long-term outcomes across studies, use of MRD status as an eligibility criterion and/or an endpoint in clinical trial design could lead to more efficient assessment of the efficacy of new drugs and combination therapies in AML," they added.

Other recent developments in AML:

[Early Palliation: Boon for AML Patients on Intensive Chemo](#)

[Stem-Cell Transplant Trial Ends in a Draw](#)

[Myeloablative Therapy Prevails in AML Transplant Study](#)

[Worse Blood Cancer Outcomes in Hispanics](#)

[Charles Bankhead](#) is senior editor for oncology and also covers urology, dermatology, and ophthalmology. He joined MedPage Today in 2007. [Follow](#) 

Comment

Infectious Disease

COVID Drug and New Mutations; Costco Offers \$29 Care; Trump Unmasked Over Bronzer

Special Reports

Can Rapid COVID Tests Reveal More Than a Positive/Negative Result?

Special Reports

When's the Best Time to Get the Updated COVID Shot?

Public Health & Policy

Nasal Sprays Recalled; 75,000 Kaiser Workers Strike; Healthcare AI May Run Amok

OB/Gyn

Ob/Gyn Accused of Sex Abuse Found Dead; Massive Medicare Scam; Veggies in the Genes?

Cardiology

'Good' Cholesterol and
Dementia Risk; Water
Allergy; Firearms Deaths
Surge in Kids

Medical News From Around the Web**STAT**

A breakthrough cystic fibrosis drug gave them the gift of time. But miracles come with complications.

HARVARD HEALTH

When — and how — should you be screened for colon cancer? -
Harvard Health

ABC NEWS

Mississippi sees 10-fold increase in babies born with syphilis since
2016: Report

CLINICAL ADVISOR

Barriers to Timely Follow-up for Heart Failure Hospitalization

THE AMERICAN JOURNAL OF PSYCHIATRY

Recent Secular Trends of Body Mass Index in Individuals With
Bipolar Disorders and in the General Population.

JOURNAL OF CLINICAL ONCOLOGY

Which Patients With Rhabdomyosarcoma Need Radiotherapy?
Analysis of the Radiotherapy Strategies of the CWS-96 and
CWS-2002P Studies and SoTiSaR Registry.

About Help Center Terms of Use Privacy Policy Do Not Sell My Personal
Information Advertise with us AdChoices  Accessibility Statement

The material on this site is for informational purposes only, and is not a substitute for medical advice, diagnosis or treatment provided by a
qualified health care provider.

© 2005–2023 MedPage Today, LLC, a Ziff Davis company. All rights reserved.

Medpage Today is among the federally registered trademarks of MedPage Today, LLC and may not be used by third parties without explicit

