

Research Uncovers Gaps and Opportunities in Acute Leukemia Care Across the Lifespan

Studies point to strategies to reduce disparities, improve outcomes and support shared decision-making.

December 20, 2021 By American Society of Hematology

Four studies presented during the 63rd American Society of Hematology (ASH) Annual Meeting and Exposition highlight opportunities to better serve the needs of patients who have not fully benefited from recent advances in [leukemia care and treatment](#).

“This briefing focuses on the most vulnerable individuals who develop leukemia – the very old and the very young, as well as people of different racial and ethnic backgrounds,” said press briefing moderator Mikkael Sekeres, MD, of University of Miami Health System. “The studies shed light on persistent disparities and how to mitigate them.”

Two studies focus on improving care for older adults with acute myeloid leukemia (AML) who have poor prognosis and limited treatment options. The first study points to gaps in communication among clinicians, patients, and families surrounding end-of-life decisions, underscoring the importance of involving patients in conversations about their care preferences early in the course of treatment.

The second study demonstrates how a new combination of drugs that targets a specific mutation in the IDH-1 gene could help improve outcomes of patients with AML while causing fewer side effects related to suppression of the immune system, potentially offering quality of life advantages in addition to enhanced response to treatment.

The final two studies examine disparities in clinical outcomes and clinical trial participation among young people with acute lymphoblastic leukemia (ALL), the most common childhood cancer. While therapeutic advances have dramatically improved survival rates for ALL, the studies suggest that factors such as race or ethnicity, socioeconomic status, and geographic location may influence access to care and clinical trials, as well as treatment outcomes. Researchers point to potential opportunities to reduce these disparities.

Study Suggests Need for Earlier Conversations About End-Of-Life Decisions for Patients With High-Risk Acute Myeloid Leukemia

[Abstract 109](#): Code Status Transitions in Patients with High-Risk Acute Myeloid Leukemia (AML)

A new study focusing on older adults with high-risk AML suggests clinicians and patients are missing opportunities to have conversations about end-of-life decisions at an early stage when patients are best equipped to discuss their options and preferences, rather than waiting until they are in the midst of a health crisis. Researchers found that only 60% of patients participated in their final code status change, a term used in health care settings to indicate the types of life-saving interventions a patient wishes to receive. This suggests that 40% were too ill to indicate their preferences about receiving life-extending measures such as resuscitation by the time the conversations occurred, leaving families and clinicians to make these critical decisions without guidance from the patient.

“The code status often reflects a deeper conversation happening between patients and clinicians about what the patient’s goals are,” said Hannah R. Abrams, MD, of Massachusetts General Hospital. “We found that patients and physicians are having these conversations very late in the course of disease. I hope that sharing this study will help both clinicians and patients bring this conversation up earlier, which could help more patients be involved in decisions at the end of life.”

The researchers analyzed the health records of 200 patients with high-risk AML to identify the timing and nature of conversations leading to code status changes. Researchers assessed transitions between full code (indicating all life-saving measures should be employed), restricted codes (such as do not resuscitate or do not intubate, which specifies the avoidance of certain measures while continuing routine treatments), and comfort measures only (limiting interventions to those intended to reduce discomfort).

The results showed the vast majority of code status changes occurred during the final weeks of life, with a median of just two days between the last code change and a patient’s death. More than half of the conversations leading to code status changes occurred when intensive life-sustaining measures were deemed futile, while just one in six were pre-emptive conversations held before a major health transition.

“It’s a hard thing to talk about, and it’s not built into our clinic visits to talk about this earlier in a patient’s course with AML,” Dr. Abrams said. Having these conversations pre-emptively during routine outpatient visits could help ensure patients have an accurate understanding of their prognosis and help clinicians align treatment strategies with the patients’ goals and preferences, Dr. Abrams noted, adding that it’s also important to have the conversation multiple times, since patients’ views and goals can change as their disease progresses. “Patients often may feel they want to readdress this with their clinicians, but they’re not sure how,” she said.

The study also found that palliative care specialists were involved in just 42% of final code transitions, suggesting future efforts could focus on ensuring optimal access to palliative care for people with high-risk AML.

Ivosidenib Combined With Azacitidine Improves Outcomes for Newly Diagnosed Acute Myeloid Leukemia With IDH-1 Mutation Compared With Azacitidine Alone

[Abstract 697](#): AGILE: A Global, Randomized, Double-Blind, Phase 3 Study of Ivosidenib + Azacitidine Versus Placebo + Azacitidine in Patients with Newly Diagnosed Acute Myeloid Leukemia with an IDH1 Mutation

In a Phase III trial, a combination of ivosidenib [Tibsovo] and azacitidine [Onureg] was found superior in treating AML as compared to azacitidine alone in terms of event-free survival, the trial's primary endpoint. The combination treatment also extended overall survival to a median of two years compared to just eight months among those receiving azacitidine alone, a three-fold increase in survival duration.

Ivosidenib is currently approved by the U.S. Food and Drug Administration (FDA) for treating relapsed or refractory AML and for newly diagnosed patients who are over age 75 or ineligible for chemotherapy and have an IDH-1 mutation. The results of the new study suggest that combining ivosidenib with azacitidine offers a promising option for newly diagnosed patients with AML who have mutations in the IDH-1 gene. Ivosidenib is targeted at IDH-1 mutations, present in about 10% of patients with AML, and works by causing leukemia cells to return to healthy cell functioning, rather than eliminating them altogether. As a result, it does not cause the same degree of myelosuppression (a decrease in the production of blood and immune cells in the bone marrow) as other combination therapies, researchers explained.

After the trial was designed, the FDA approved venetoclax [Venclexta] as a first line treatment in this patient group, making the combination of azacitidine and venetoclax the current standard of care for AML patients ineligible for intensive chemotherapy throughout much of the world. Although the new trial does not directly compare the ivosidenib-azacitidine combination with the venetoclax-azacitidine standard of care, researchers said that the study sheds light on ivosidenib-azacitidine as a treatment option that could prove particularly useful for the hard-to-treat subset of AML patients with IDH-1 mutations, who were the target of the study.

"This high-risk population still needs improved strategies to prevent relapse or improve the response to front-line treatment," said Stephane de Botton, MD, PhD, of Institut Gustave Roussy in France. "Because of this drug's mechanism of action, we were able to show a significant increase in the rate of complete response and improvement in symptoms without any increase in complications related to immunosuppression and infection."

The trial enrolled 146 patients in more than 20 countries with newly diagnosed AML. All patients had IDH-1 mutations and were ineligible for intensive induction chemotherapy, typically due to age or frailty. Half of the participants received ivosidenib and azacitidine while half received azacitidine and a placebo. The primary endpoint of the AGILE trial was event-free survival, which was statistically significant in favor of the ivosidenib arm, with a hazard ratio of 0.33.

Median overall survival was approximately three times longer in the ivosidenib arm, at 24 months, compared with a median of 7.9 months among those receiving azacitidine alone. Patients

receiving ivosidenib were also significantly more likely to achieve a complete response to treatment, which occurred in 47% of patients receiving ivosidenib and just 16% of those receiving azacitidine alone.

The trial also found a favorable safety profile for ivosidenib, with rates of adverse events similar to those seen with azacitidine alone. “In addition, our results showed a significant improvement in quality of life with the ivosidenib combination therapy, which is a measure that is very important for patients,” said Dr. de Botton.

The study was stopped early after preliminary results indicated the ivosidenib-azacitidine combination yielded substantial benefits over azacytidine alone.

Study Finds Persistent Racial Disparities in Acute Lymphoblastic Leukemia Survival

[Abstract 211](#): Racial, Ethnic, and Socioeconomic Factors Result in Disparities in Outcome Among Children with Acute Lymphoblastic Leukemia Not Fully Attenuated By Disease Prognosticators: A Children’s Oncology Group (COG) Study

A study of nearly 25,000 young people with ALL reveals significant gaps in survival rates between white, Hispanic, and Black patients, as well as worse outcomes among those of lower socioeconomic status. Biological or genetic factors accounted for some, but not all, of the disparity.

“Our study shows that race and ethnicity-based disparities continue to exist and are substantial,” said Sumit Gupta, MD, of The Hospital for Sick Children (SickKids) in Toronto, Canada. “All groups do well overall, but some do substantially better than others. There is an urgent need to examine the factors leading to these different outcomes among different racial and ethnic groups.”

The researchers analyzed health records of 24,979 patients diagnosed with ALL at age 30 or younger who enrolled in clinical trials of the Children’s Oncology Group (COG) between 2004 and 2019. COG, part of the National Cancer Institute Clinical Trials Network of the National Institutes of Health, is the world’s largest organization devoted exclusively to childhood and adolescent cancer research.

White patients on average had a five-year event-free survival rate of 87.4%, compared with 82.8% for Hispanic patients and 81.9% for Black patients. In the U.S., patients on Medicaid, an indicator of low socioeconomic status, had a five-year event-free survival rate of 83.2% compared with 86.3% among U.S. patients not on Medicaid. The analysis showed similar patterns for overall survival rates, although the magnitude of the disparities in overall survival was higher.

While some genetic mutations in leukemia cells differed between racial and ethnic groups, they did not fully account for the observed differences in survival. “Based on the data, it is unlikely that leukemia biology fully explains these disparities,” said Dr. Gupta. Differences in socioeconomic status among racial groups also do not fully explain the racial disparities, he noted.

Dr. Gupta said research to determine the specific reasons for these disparities is needed, particularly looking at the role of differences in access to health care, in treatments offered, or in the types of support children and families receive during cancer treatment. Since the study focused on young people who were enrolled in clinical trials, which implies a certain level of access to care, he said the racial disparities observed in the study may be even more pronounced in the general population.

Study Reveals Mismatch Between Racial Diversity of Clinical Trial Participants and Young Patients With Acute Lymphoblastic Leukemia in the U.S.

Abstract 337: Enrollment Characteristics and Outcomes of Hispanic and Black AYA ALL Patients Enrolled on a U.S. Intergroup Clinical Trial: A Comparison of the CALGB 10403 (Alliance) Cohort with U.S. Population-Level Data

A study of young people with ALL across the U.S. found that Hispanic patients were significantly underrepresented in a large clinical trial compared with the general patient population. The study also found that Hispanic patients in the trial had leukemia outcomes on par with non-Hispanic white participants, suggesting that clinical trial participation can help to mitigate some of the racial and ethnic disparities in cancer outcomes observed in the overall population, further underscoring the need to ensure appropriate racial diversity in cancer clinical trials.

“It is an ongoing problem in cancer research that we repeatedly see a significant mismatch between clinical trial participants and what is happening in the real world,” said Lori Muffly, MD, MS, of Stanford University School of Medicine. “We have to do more to align our clinical trial participants with the epidemiology of disease across this country.”

The researchers analyzed health outcomes, socioeconomic status, and race and ethnicity among 295 adolescent and young adult (AYA) patients enrolled in CALGB 10403, a clinical trial for a treatment regimen designed specifically for younger patients that was found superior to a regimen used for older patients. They then compared the CALGB data with data from cancer registries reflecting the overall incidence (the North American Association of Cancer Registries) and overall survival (SEER registry) of patients with ALL from different racial and ethnic groups in a similar age range.

The results show a striking difference between clinical trial participants and the general population; while 41.7% of U.S. AYA patients with ALL were Hispanic, only 16.3% of CALGB 10403 participants were Hispanic. In part, this difference was explained by the fact that the study did not enroll patients in some states that have a high proportion of Hispanic residents, such as Texas and Florida. However, researchers found Hispanic participants were underrepresented in each state where the trial did open compared with the proportion of Hispanic patients in the broader population for that state.

The study also found that Hispanic patients who participated in CALGB 10403 had high rates of compliance with trial protocols and outcomes that were similar to those for non-Hispanic white participants, despite having a higher likelihood of genetic markers associated with worse ALL

outcomes. This contrasts with SEER registry data that showed Hispanic patients in the general population suffered significantly worse outcomes than non-Hispanic white patients.

“For diseases that heavily affect certain racial or ethnic groups, putting thought into where those patients are located and where trials open could help,” said Dr. Muffly. “These findings should generate conversations about how we can do better.”

The researchers found different trends among Black patients, who comprised a much smaller proportion of patients in both CALGB 10403 and the broader AYA ALL population. The proportion of Black patients in the clinical trial (6.4%) was roughly the same as the proportion in the patient population broadly (8.5%), and Black patients saw significantly worse outcomes across the board, a finding researchers said warrants further investigation.

This [press release](#) was published by the American Society of Hematology on December 11, 2021.

© 2026 Smart + Strong All Rights Reserved.

<http://beta.docker.tusaludmag.com/article/research-uncovers-gaps-opportunities-acute-leukemia>