Advances in Technology Help Improve Safety and Access to Blood Cancer Therapies

Emerging tests and treatment strategies guide more tailored approaches and ease the burden on patients.

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ORLANDO — Four clinical trials to be presented at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition illustrate how advancements in technology are contributing to an improved outlook for many patients with blood cancers.

“These studies tie together different approaches bringing technological improvements to bear on therapeutic innovation and improving patient safety,” said Wendy Stock, MD, Anjuli Seth Nayak Professor of Medicine at the University of Chicago Medicine, who moderated the press briefing The Next Wave of Innovation: Breakthrough Blood Cancer Trial Findings. “They also show how new drugs and technologies can reduce toxicity and make curative therapies feasible and accessible to a broader population of patients.”

The first study suggests that patients with chronic lymphocytic leukemia do not necessarily need to remain on therapy indefinitely, as fixed-duration combination treatments resulted in outcomes that were inferior to continuous treatment with a single agent. The study compared continuous ibrutinib [Imbruvica] alone versus an approximately one-year course of either venetoclax [Venclexta] and ibrutinib or venetoclax and obinotuzumab [Gazyva].

The second and third studies point to the power of using sensitive tests for detection of measurable residual disease (MRD) as an early predictor of outcomes and to inform treatment decisions in patients with acute leukemias. In the second study, MRD positivity following two cycles of intense chemotherapy was found to be strongly associated with worse outcomes among patients with acute myeloid leukemia (AML), regardless of MRD assessment method. The results could help guide the adoption of MRD as a biomarker to inform patient care, and the study also provides evidence for the use of MRD as an early surrogate endpoint of survival for clinical trials in AML.

The third study used MRD testing to identify patients at very low risk of relapse after initial

treatment for B-cell acute lymphoblastic leukemia and then assessed outcomes from different conditioning regimens before hematopoietic cell transplantation. Patients had similar outcomes with chemotherapy-based conditioning versus total body irradiation, suggesting that patients who are low-risk can safely avoid the long-term side effects of total body irradiation with a chemotherapy-based regimen.

In the final study, researchers found that receiving a post-transplant cyclophosphamide-based graft-versus-host disease prevention strategy can overcome the negative effects previously associated with receiving a bone marrow transplant from an unrelated and genetically mismatched donor. Based on the findings, researchers say many patients could safely receive transplants from a much broader pool of potential donors, improving access to this curative therapy.

Continuous and Fixed-Duration Treatments Result in Similar Outcomes for CLL
1: Fixed-duration versus continuous targeted treatment for previously untreated chronic lymphocytic leukemia: Results from the randomized CLL17 trial

According to a new trial, patients with chronic lymphocytic leukemia (CLL) show comparable outcomes whether they receive a single-agent treatment indefinitely or a combination treatment for a fixed period of time.

The study is the first prospective trial to directly compare these two approaches. With a median follow-up of nearly three years, the results show these approaches are essentially equivalent in terms of risk of death or disease progression.

“As clinicians, we often assume that continuous treatment will always be more effective because you’re simply giving more treatment, but this study shows that is not necessarily the case,” said lead study author Othman Al Sawaf, MD, a hematologist and medical oncologist at the University of Cologne in Germany. “The results provide the first evidence that fixed-duration treatment, which patients often prefer, is indeed non-inferior to continuous treatment, suggesting clinically equal efficacy.”

CLL is the most common adult leukemia in which abnormal white blood cells grow out of control and build up in the bone marrow Three classes of agents have been developed that target CLL: Bruton tyrosine kinase (BTK) inhibitors, BCL2 inhibitors, and CD20 antibodies. Recommended treatment regimens for newly diagnosed CLL fall into two main categories: indefinite continuous treatment with a BTK inhibitor or a fixed-duration treatment, typically lasting about a year, using a combination of a BCL2 inhibitor and CD20 antibody or BTK inhibitor.

To compare these approaches, researchers randomly assigned 909 adult patients to one of three regimens. Those assigned to the “I” arm received continuous ibrutinib (a BTK inhibitor) indefinitely unless they experienced disease progression or unacceptable side effects. Those in the “VO” arm received 12 cycles of venetoclax (a BCL2 inhibitor) with a course of obinutuzumab (a CD20 antibody) added during the first six cycles. Those in the “VI arm” received 12 cycles of venetoclax

following three cycles of ibrutinib.

At the time of analysis, the median follow-up period was 34 months, with a range of zero to 49 months. The rates of progression-free survival were 81% in the I arm, 81.1% in the VO arm, and 79.4% in the VI arm. Between-group differences fell below the pre-specified threshold for non-inferiority, meeting the study's primary endpoint for this time point.

The three arms also showed similar results in terms of overall response to treatment and overall survival, with overall response rates ranging from 84.2% to 88.5% and overall survival ranging from 91.5% to 96.0%.

The group receiving continuous ibrutinib treatment had a lower rate of complete response to treatment, an endpoint that was achieved in only 8.3% of the I arm compared with 51.5% in the VO arm and 46.2% in the VI arm. In addition, none of the patients receiving continuous ibrutinib achieved the status of undetectable measurable residual disease (MRD), a biomarker indicating that all or nearly all cancer cells have been eliminated. By contrast, undetectable MRD was achieved in 73% and 62% of patients as measured in the blood, and 62% and 40% of patients as measured in the bone marrow for the VO and VI arms, respectively.

"The secondary endpoints are surrogate parameters for us to assume long-term efficacy," said Dr. Al Sawaf. "With the fixed-duration paradigm, we see higher rates of complete response and MRD responses, and with the continuous single-agent treatment we see lower complete response and MRD responses."

Rates of side effects were overall similar across study arms, with the most common issues being infections and gastrointestinal disorders. Blood and lymphatic system disorders, cardiac disorders, and second cancers were also somewhat frequent across all arms.

Subgroup analyses showed that cardiovascular issues were more common among patients who received ibrutinib, especially among those who took ibrutinib for a longer duration. Obinutuzumab was associated with a higher risk of severe infections and with a shorter progression-free survival among patients with aggressive forms of CLL.

Researchers said that the ongoing follow-up within the trial will help strengthen the evidence for any differences in performance between the different treatment approaches. In addition, Dr. Al Sawaf said that other studies are underway to identify biomarkers that might help doctors determine which patients are most likely to benefit from each treatment strategy.

The study was investigator-initiated under sponsorship of the University of Cologne; AbbVie Inc., Janssen Pharmaceuticals, and Roche Pharmaceuticals provided the study drugs and funding to support the trial conduct; parts of the analyses and research staff were supported by the German Research Foundation (Deutsche Forschungsgemeinschaft).

This study was simultaneously published in The New England Journal of Medicine.

Othman Al Sawaf, MD, of the University of Cologne, will present this study on Sunday, December 7, 2025, at 2:05 p.m. Eastern time during the Plenary Scientific Session in West Hall D2 of the Orange County Convention Center.

Measurable Residual Disease Shows Strong Potential as an Early Indicator of Survival in Patients with Acute Myeloid Leukemia
343: Validation of measurable residual disease as a surrogate endpoint in acute myeloid leukemia: A HARMONY Alliance study of European randomized trials

Sensitive tests designed to detect very small numbers of remaining leukemia cells after treatment, known as measurable residual disease (MRD), may provide an early and reliable indicator of long-term outcomes for patients with acute myeloid leukemia (AML), according to a new study from the HARMONY Alliance.

The study is the first to evaluate MRD as a potential measure of treatment efficacy and outcome prediction in the context of AML. The results suggest that MRD could help refine how physicians assess treatment response and personalize post-remission care. The findings may also help regulators determine whether MRD can serve as an intermediate endpoint for clinical trials of new AML therapies, providing an earlier signal of treatment benefit.

AML is a cancer that occurs in the bone marrow, causing an overproduction of abnormal white blood cells and impeding the production of healthy blood cells. MRD is an established biomarker in several blood cancers and is increasingly used to guide therapy. The U.S. Food and Drug Administration (FDA) has already accepted MRD as a surrogate endpoint in clinical trials for multiple myeloma, which can help speed regulatory approvals for new therapies since MRD can typically be assessed years earlier than survival outcomes. However, the FDA has not approved MRD as a surrogate endpoint for AML.

To assess the reliability of MRD as an early predictor of survival for AML at the individual and trial levels, researchers analyzed data from 1,858 patients who underwent MRD tests as part of their participation in seven prospective clinical trials conducted by four European cooperative groups. At the individual-patient level, those who tested MRD-positive after two cycles of intensive chemotherapy were less than half as likely to survive as those who were MRD-negative. This strong association held true regardless of the assigned study arm or MRD testing method.

“The individual-level association is pretty striking – MRD positivity remains an independent predictor of worse outcomes,” said Jesse Tettero, MD, PhD, who led the research while at Amsterdam University Medical Center Department of Hematology in the Netherlands. “It provides stronger prognostic information than any single genetic or molecular marker we currently use. The association was very consistent, even after adjusting for other clinical factors, which really confirms the patient-level link between MRD and survival.”

At the trial level, the analysis showed that treatment effects on MRD closely mirrored those on overall survival, particularly among patients who did not receive a hematopoietic cell transplant

(HCT). The correlation between MRD improvement and survival benefit was high, but the confidence interval for this association fell below the study's predefined threshold for this endpoint. In addition, the relatively small number of available randomized trials limited the precision of this estimate.

"For the trial-level surrogacy, the data for non-transplanted patients show a strong correlation, but caution is warranted due to the number of trials. Trial-level surrogacy is a very high bar to reach," said Dr. Tettero.

Regulators could consider accepting MRD as an intermediate endpoint rather than a full endpoint. In this case, data on MRD status could be used as a basis for provisional approval while the study continues and survival data matures. "This could speed AML drug development without compromising the quality of evidence. That may be a reasonable implementation," said Dr. Tettero.

The results revealed HCT could modify the relationship between MRD and long-term outcomes. MRD is typically measured shortly after a patient completes initial treatments – a point in time that is before patients would receive a transplant – yet HCT strongly affects outcomes because it is a curative therapy in most cases, influencing the trial-level surrogacy.

Researchers noted that not all MRD tests are equal. High-volume reference centers using standardized methods produce the most reliable results, while decentralized, low-volume testing can be less consistent.

"The quality of MRD testing really depends on where and how it's done. Centralized, experienced laboratories deliver accurate and reproducible results, which are essential if MRD is to be used for clinical or regulatory decisions. I think the field has really developed and matured, so people are becoming more interested in using MRD," said Dr. Tettero.

The study was conducted within the HARMONY Alliance, a European public-private partnership funded by the European Union.

Jesse Tettero, MD, of Virginia Tech FBRI Cancer Research Center, will present this study on Saturday, December 6, 2025, at 4:00 p.m. Eastern time in Valencia Room W415A of the Orange County Convention Center.

Chemotherapy and Radiation Are Comparable as Pre-Transplant Conditioning for Patients with B-acute Lymphoblastic Leukemia Who Have No Measurable Residual Disease

163: High event-free (EFS) and overall survival (OS) after non-total body irradiation (TBI) conditioning and allogeneic hematopoietic cell transplantation (HCT) in next-generation-sequencing minimal residual disease (NGS-MRD) negative B-acute lymphoblastic leukemia (B-ALL): Results from the EndRAD trial (PTCTC ONC1701)

In a new trial, patients with B-acute lymphoblastic leukemia (B-ALL) who had no evidence of

remaining cancer cells after prior treatment, experienced comparable outcomes whether they received chemotherapy-based conditioning or total body irradiation (TBI), the standard conditioning regimen used before hematopoietic cell transplantation. The findings could allow more patients to avoid TBI and its associated long-term side effects.

The study is the first to test the use of chemotherapy-based conditioning in patients with no evidence of measurable residual disease (MRD) through next-generation-sequencing (NGS) before starting the pre-transplant conditioning process. The trial met its primary endpoint with a two-year relapse-free survival rate comparable to that of an observational cohort of patients who received TBI-based conditioning.

“We used NGS-MRD – a very sensitive method to identify any residual leukemia cells in the patient – to categorize patients who are at very low risk for relapse and pilot the use of non-TBI-based conditioning versus the standard TBI conditioning,” said lead study author Hisham Abdel-Azim, MD, division chief for transplant/cell therapy and hematological malignancies and professor of pediatrics, medicine and basic sciences at Loma Linda University School of Medicine in California. “Using our approach, we were able to save a significant portion of patients who were MRD-negative before transplant from having to receive TBI without compromising their outcome.”

B-ALL is a cancer of the bone marrow that causes a buildup of abnormal B-cells, a type of white blood cell. It is the most common type of childhood leukemia and most common subtype of ALL in adults. Allogeneic hematopoietic cell transplantation is a curative treatment for B-ALL that is commonly recommended for patients at high risk for relapse. Before a transplant, patients must undergo a conditioning regimen of intensive chemotherapy and radiation to clear the bone marrow and make space for the transplanted cells. Although previous studies suggest TBI-based conditioning results in better outcomes than chemotherapy conditioning in general, TBI is also associated with long-term detrimental impacts on memory, endocrine function, and subsequent cancers.

The study used NGS of IgH B-cell receptor rearrangements (NGS-MRD) to identify patients who have no detectable cancer, which researchers hypothesized would make them good candidates for chemotherapy-based conditioning without raising the risk of relapse.

In total, 51 MRD-negative patients were enrolled in the study and received transplants with chemotherapy-based conditioning. Participants’ age at the time of their initial B-ALL diagnosis ranged from 2 to 30 with a median age of 13.5 years. Half of the enrolled patients were male. When they received their transplant, half were on their first complete remission after initial treatments and half were on their second complete remission.

To date, participants have been followed for a median of 2.3 years with a range of several months to six years. Researchers compared patients’ outcomes to those of an observational cohort of 151 patients who received the standard TBI conditioning.

At just over two years, 82% of those who received chemotherapy-based conditioning were alive,

and 76.3% were alive without experiencing a relapse. Twelve percent of participants died from causes other than a cancer relapse, and 12% experienced a relapse.

Event-free survival and overall survival were similar in the TBI and non-TBI cohorts.

Based on the findings, researchers said that the NGS-MRD test can be a useful biomarker for identifying patients who can safely avoid TBI conditioning. “This study really sets a new standard of care for those patients,” said Dr. Abdel-Azim. “Using this guided approach, patients who are NGS-MRD negative prior to transplant could be getting non-TBI based conditioning.”

Graft-versus-host-disease (GVHD) is a common complication of hematopoietic cell transplantation that occurs when transplanted cells attack a patient’s own cells. Ten percent of patients experienced grades 3-4 acute GVHD and 21% experienced chronic GVHD requiring systemic treatment.

Younger age at diagnosis and younger age at the time of hematopoietic cell transplantation were associated with inferior outcomes. Among patients who were NGS-MRD negative, outcomes were similar among those with high-risk and non-high-risk genetic abnormalities.

The researchers plan to further investigate genetic abnormalities and other factors that may influence outcomes in order to guide decisions about which conditioning regimen to recommend based on a patient’s particular risk profile.

The study was funded by the Gateway for Cancer Research.

Hisham Abdel-Azim, MD, of Loma Linda University School of Medicine Cancer Center, will present this study on Saturday, December 6, 2025, at 12:00 noon Eastern time in W331 of the Orange County Convention Center.

Protective Regimen Allows Successful Stem Cell Transplant Even Without Close Genetic Match Between Donor and Recipient
936: Mismatching of unrelated donors beyond a single HLA-locus does not adversely impact outcomes at one year following transplantation: Results from the NMDP sponsored ACCESS study

A new study shows that giving the chemotherapy drug cyclophosphamide after allogeneic hematopoietic cell transplantation, a curative treatment for common types of blood cancer, can make the procedure safe and effective even when donors and recipients are unrelated and have extensive genetic mismatches. Historically, genetic compatibility has played a primary role in identifying matched donors; these results suggest that many patients who need a transplant could now have access to a much broader pool of potential donors and expect outcomes comparable to those from fully matched donors.

The study found that one-year survival was similar whether patients received transplants with more or less extensive genetic mismatches. Rates of graft-versus-host disease (GVHD), a

complication in which donor cells attack the recipient's own cells, were also comparable.

"With a post-transplant cyclophosphamide-based GVHD prevention strategy, outcomes following mismatched unrelated donor transplant are similar to those achieved with matched donors," said senior author Antonio Jimenez-Jimenez, MD, associate professor of medicine in the division of transplantation & cellular therapy at Sylvester Comprehensive Cancer Center, part of the University of Miami Miller School of Medicine. "This allows us to find donors for virtually everyone, regardless of their ancestry. Roughly 99% of patients will now have access to a suitable donor on international registries."

Donor-recipient compatibility has long been assessed by counting how many human leukocyte antigens (HLA) markers a donor and recipient share. These markers encode proteins that serve as immune system receptors on cell surfaces. Matching eight HLA markers has historically produced the best results, whereas having fewer matched markers has been associated with lower survival and higher rates of GVHD.

Finding a donor with close HLA matching is especially challenging for people of non-European ancestry; for example, a Black patient's likelihood of finding a fully matched donor is just 29%, compared with 89% among non-Hispanic white patients.

Previous studies have shown that giving cyclophosphamide after transplant can improve outcomes when donors and recipients are related but have HLA mismatches, and the same group of investigators has reported encouraging results using bone marrow grafts. This new study is the largest to evaluate the approach in unrelated donors with only four to seven of eight matched HLA markers, using peripheral hematopoietic cell grafts. Peripheral hematopoietic cell grafts are the most common source for hematopoietic cell transplantation and use an outpatient collection process akin to a blood donation.

Among the 268 adult participants, 183 had seven matched HLA markers with their donors, and 85 had four to six. At one year, 79% of the seven-match group and 86% of the four-to-six match group were alive, the study's primary endpoint. Rates of GVHD-free, relapse-free survival (51% and 55%), relapse (17% and 23%), and non-relapse mortality (14% and 8%) were also similar.

The results suggest that when selecting hematopoietic cell donors, doctors may be able to broaden the acceptable range of HLA matching – greatly expanding the pool of potential donors for each patient – and place greater emphasis on other factors known to influence outcomes, such as younger donor age. "This allows us to try to optimize other donor characteristics beyond just HLA matching," said Dr. Jimenez-Jimenez.

The results were comparable to those reported by the same investigators in a previous study that used bone marrow grafts for similarly mismatched unrelated donor transplants, suggesting that peripheral blood grafts can be safely and effectively used in this setting. "This makes transplantation much more accessible and easier for patients, and even safer for donors," said Dr. Jimenez-Jimenez.

The two study groups had comparable and relatively low rates of GVHD. Acute grade 2-4 GVHD occurred in 39% of patients with seven of eight matched markers and 34% of those with four to six matched markers at six months. Rates of moderate-to-severe chronic GVHD at one year were 11% and 8%, respectively.

Patients with fewer matched markers had a slightly higher rate of primary graft failure, meaning that the transplanted cells did not begin producing healthy blood cells. This occurred in 3% of recipients with seven matched alleles and 7% of those with four to six matches, and was limited to older adults who received reduced intensity conditioning. Researchers plan further analyses to better understand and prevent graft failure in this subgroup.

Dr. Jimenez-Jimenez noted that the study was not a randomized trial and that larger studies will be important to confirm these findings. Several related efforts are already underway, including a companion study of pediatric bone marrow transplant recipients and a trial focused on refining the dosing of this cyclophosphamide-based GVHD prevention strategy to reduce toxicity while maintaining its benefits.

Antonio Jimenez-Jimenez, MD, of the University of Miami School of Medicine, will present this study on Monday, December 8, 2025, at 4:00 p.m. Eastern time in W331 of the Orange County Convention Center.

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