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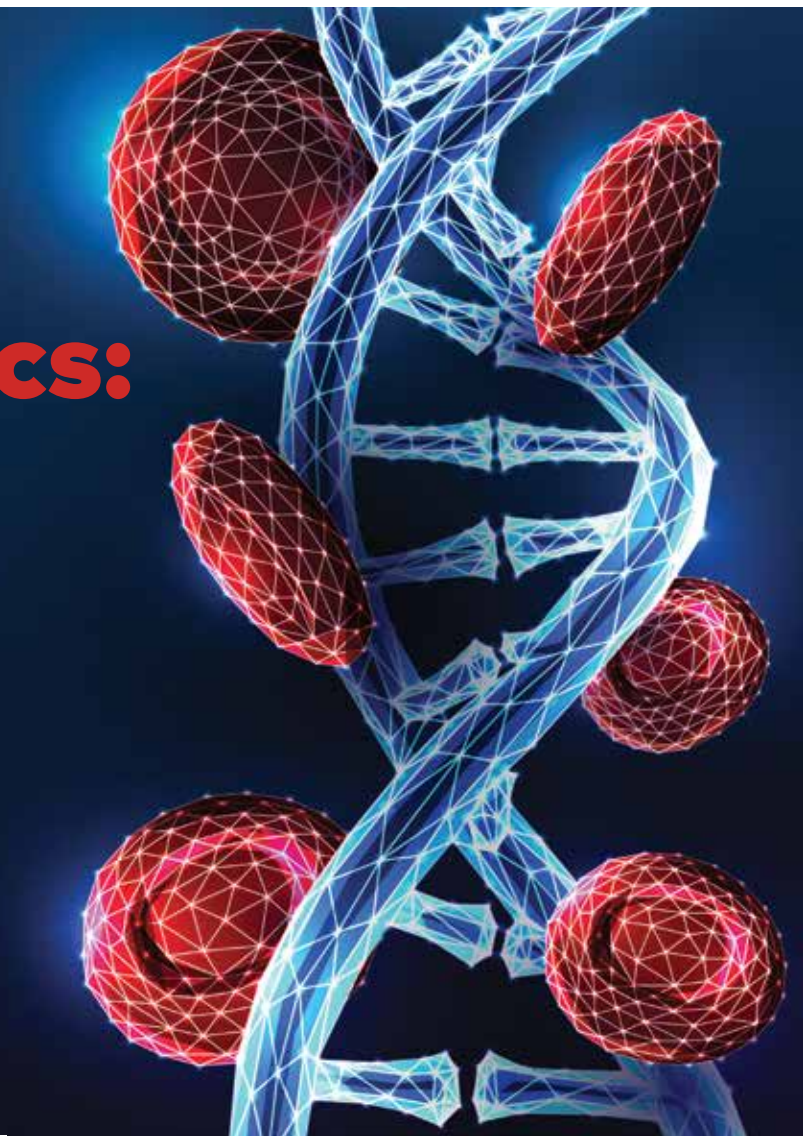
Precision Diagnostics:

Continued Incremental Integration Into Hematologic Malignancy Management



With expert opinions from **Manni Mohyuddin, MD, Justin M. Balko, PharmD, PhD, Natalie S. Grover, MD,** *and more.*

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When the Backbone Becomes the Platform: Rethinking Induction in AML

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Alex McDonald, MD, explains how physicians can navigate polarized health conversations by replacing sound bites with nuance, curiosity, and trust—turning disagreement into connection with practical strategies that strengthen patient relationships and improve outcomes.

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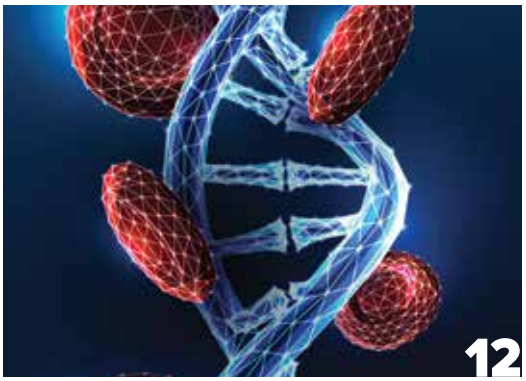

Precision Diagnostics:

Continued Incremental Integration Into Hematologic Malignancy Management

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Complementary and Alternative Medicine and Integrative Oncology in Hematology

*By **Kimberly Ku, MD***

The NIH National Center for Complementary and Integrative Health provides the foundational taxonomy[1] in which complementary and alternative medicine (CAM) represents nonmainstream practices alongside conventional medicine, alternative therapies are used *in place* of such, and CAM includes the two together, which has led to further need to better distinguish this terminology.

The Society for Integrative Oncology (SIO), in collaboration with the American Society of Clinical Oncology (ASCO), defines integrative oncology (IO) as "a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment."[2,3]

The SIO-ASCO guidelines deliberately use the term *integrative therapies* rather than *complementary therapies* to emphasize that these modalities are intended to be fully integrated into routine oncology practice, not treated as add-ons or afterthoughts. Hence, the shift from CAM to IO language reflects a maturation of the field respecting patient-reported outcomes (PROs). When a clinician practices IO, they are selectively recommending modalities with evidence of support while actively screening for and counseling against harmful alternatives or drug interactions.[2,4,5]

Notably, the SIO-ASCO guidelines span multiple domains—including pain management, anxiety/depression, fatigue, breast cancer, and use of cannabinoids—establishing IO as a guideline-supported subspecialty rather than a fringe practice, acknowledging the significance of PROs.[2,3,6] The National Comprehensive Cancer Network (NCCN) Adolescent and Young Adult guidelines also explicitly recommend assessing patients' use of both "integrative therapies and complementary and alternative medicine" and referring interested patients to IO specialists.[7]

Interestingly, data suggest important differences in IO practices in hematology compared with solid tumor oncology, particularly in how patients access palliative and integrative support. A large survey at the Sidney Kimmel Cancer Center revealed that hematologic cancers were the second most common malignancy (20.9%) among patients expressing interest in IO, with 71.3% of all respondents expressing interest in an IO consultation. Yet, 66.8% reported IO was never discussed during their care.[8]

Comparative palliative care utilization between patients treated in the realm of hematologic versus solid organ cancers reveal the following disparities, which may lead to important lessons for practice improvement. In patients with hematologic malignancies, we observe:

- Lower palliative care referral rates: 40.4% versus 55.6% in a large German population study, with referrals occurring later (34 vs 50 days before death).[9]
- Higher rates of aggressive end-of-life care: more hospitalizations, ICU admissions, in-hospital deaths, and shorter hospice stays.[10, 11]
- A Swedish nationwide study confirmed that only 42% of patients with a hematologic malignancy received specialized palliative care versus 54% of patients with a solid tumor ($P<0.001$), with significantly poorer symptom relief.[12]
- Physicians cited palliative care as "not meaningful" for 35.1% of patients with hematologic cancer versus only 5.3% for patients with breast cancer.[13]

The 2024 ASCO Palliative Care Guideline update now explicitly recommends that patients with advanced hematologic malignancies should be referred to specialized palliative care teams early, acknowledging the historical underutilization of palliative care in this population.[11]

Several factors contribute to the disparity in integrative and palliative support for hematology patients. Some factors may include prognostic uncertainty because hematologic malignancies often lack clear transitions between curative and palliative phases, making referral timing difficult[10,11] and resistance to a palliative referral when curative intent remains.[10] Hematologists may self-manage palliative tasks more frequently than oncologists who are more likely to delegate to palliative care specialists.[14] Finally, nondisclosure can be a factor: up to 60% of hematology patients do not inform their physicians about CAM use, citing fear of rejection or the perception that physicians are indifferent.[15]

The SIO-ASCO guidelines recommend several integrative modalities applicable to hematology patients, including acupuncture, massage, mindfulness-based interventions, and yoga for treatment of anxiety, depression, and reflexology for

relief of general cancer pain.[16, 17] A dedicated review of the use of acupuncture for patients with hematologic malignancies revealed that the strongest evidence for its use is in the relief of pain and nausea/vomiting, with emerging data for fatigue, insomnia, and peripheral neuropathy.[18] For patients with lymphoma specifically, data on acupuncture, touch therapy, mind-body interventions, and certain dietary supplements to address pain, neuropathy, fatigue, and insomnia are available.[19]

The NCCN Palliative Care Guidelines explicitly recommend considering nonpharmacologic and integrative interventions, including cognitive behavioral therapy, massage, and art or music therapy, as part of shared decision-making for all patients with cancer, including those with hematologic malignancies.[20]

This article is part 1 of a series by Kimberly Ku, MD. Go to bloodcancerstoday.com to read the full story.

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When the Backbone Becomes the Platform: Rethinking Induction in Acute Myeloid Leukemia

Amer M. Zeidan,
MBBS, MHS

For most of the last 50 years, the conversation with a patient with newly diagnosed acute myeloid leukemia (AML) who is fit for intensive chemotherapy (IC) has followed a familiar script. The goal of therapy is cure, but to achieve this goal, we have to give IC, with the caveat that IC is associated with prolonged hospitalization and risk for serious complications. For older and unfit patients, the discussion was different: the goal was to improve quality of life and potentially survival, but without a cure prospect. This lower-intensity therapy (LIT) approach used a hypomethylating agent (HMA), or low-dose cytarabine, for almost the last 20 years and was redefined with the addition of venetoclax for the last several years.

Over the years, additional adjustments to these two divergent approaches included combining targeted agents with either IC or LIT backbones. However, the therapeutic intent often remained binary: IC with or without allogeneic hematopoietic stem cell transplantation (HSCT) as a curative approach or LIT with HMA plus venetoclax as a palliative approach. However, the landscape started to shift, and the two approaches started to intertwine.

The PARADIGM study, presented at the 67th American Society of Hematology Annual Meeting & Exposition, was a randomized phase 2 trial that challenged this dogma and showed that a LIT regimen with the HMA azacitidine plus venetoclax (aza-ven) can potentially outperform IC in some patients who are otherwise eligible for IC. PARADIGM enrolled 172 adults randomized 1:1 to receive aza-ven or IC (7+3 or CPX-351 [cytarabine and daunorubicin]). Median event-free survival (EFS) was 14.6 months with aza-ven versus 6.15 months with IC, and the 1-year EFS rates were 53.4% versus 36.0%, respectively. A greater proportion of patients who received aza-ven subsequently proceeded to HSCT, and although the decision to proceed to HSCT was left to treating physicians, the EFS advantage of aza-ven remained significant even after adjusting for HSCT in multivariable models.

Further, aza-ven had a better safety profile and shorter hospitalization duration than IC. None of the patients who received aza-ven required ICU admission in the first 30 days, versus nearly 10% in the IC arm. Importantly, patient-reported outcomes suggested better quality of life, symptom burden, and depression scores in the aza-ven group.

The investigators of PARADIGM should be congratulated for designing and conducting an investigator-initiated randomized study to address such a critical clinical question. The design of any clinical trial is a balance between what is ideal and what is feasible. The findings should not be taken at face value when applied to today's clinical practice without considering the significant caveats that require careful interpretation. PARADIGM excluded important subsets of newly diagnosed and fit patients with AML, such as those with core binding factor (CBF) AML and *FLT3* mutations and younger patients with *NPM1* mutations. Therefore, PARADIGM's findings do not extend to these patients. Ongoing randomized studies are comparing the addition of FLT3 inhibitors with either IC or aza-ven for patients with *FLT3* mutations who are fit for IC.

Furthermore, the PARADIGM population was predominantly European LeukemiaNet (ELN) adverse risk (72%), which is exactly the group in which IC is expected to yield the most disappointing long-term results and in which many leukemia experts have already shifted to using aza-ven induction followed by HSCT for many fit patients with AML. Caution should also be exercised when evaluating EFS as a practice-changing end point in AML studies that use aza-ven because EFS has

not been well validated as a surrogate end point for overall survival (OS). In this study, although median OS numerically favored aza-ven (21.5 vs 18.6 months), the difference did not reach statistical significance.

These details matter. Some oncologists will read just the topline results that aza-ven beats IC in fit patients with newly diagnosed AML, and some will apply it broadly, including to younger patients with *FLT3* mutations, to patients with CBF leukemia, to younger patients with *NPM1*-mutated AML—populations that were excluded in which many patients will not proceed to HSCT. The PARADIGM findings apply to a specific, relatively high-risk subset of IC-eligible patients, and even within that group, the benefit appears most pronounced when aza-ven is used to bridge to HCT. For ELN intermediate-risk fit patients who will not proceed to transplant, we do not have evidence that aza-ven is superior to IC as a standalone strategy. Although some experts will recommend that all ELN intermediate-risk patients should undergo HSCT when possible, others take a more nuanced approach based on the specific genetic profile and potentially measurable residual disease measurements. The PARADIGM trial should be followed by a confirmatory phase 3 trial with OS as the primary end point and potentially include more ELN intermediate-risk patients.

Another ongoing study addresses older and less fit patients with AML who cannot tolerate intensive induction. The phase 2 ASCERTAIN-V trial, which I presented on behalf of the investigators at ASCO 2025 (the American Society of Clinical Oncology Annual Meeting), evaluated an all-oral regimen of decitabine-cedazuridine (DEC-C) plus venetoclax in 101 patients with newly diagnosed AML aged 75 years and older or younger patients with comorbidities precluding IC. DEC-C, an oral, fixed-dose formulation combining decitabine 35 mg and cedazuridine 100 mg, was designed to replicate the pharmacokinetic exposure of IV decitabine, with cedazuridine used to inhibit intestinal cytidine deaminase degradation. At a median follow-up of 11.2 months, the complete remission (CR) rate was 46.5%, the CR or CR with incomplete hematologic recovery rate was 63.4%, and the median OS was 15.5 months. Among patients achieving CR, 75.3% remained in remission at 1 year. Although cross-trial comparisons should always be considered with caution, the efficacy and safety are comparable with those seen with parenteral aza-ven in VIALE-A.

The appeal here is obvious: a two-pill regimen, taken at home, eliminates the monthly 7-day clinic visits required for parenteral azacitidine administration. For an older patient with limited mobility or a long commute to an academic center, that logistical shift is important: it is the difference between treatment that is theoretically accessible and treatment that is actually feasible and could reduce what we commonly refer to as *time burden* or *time toxicity*—the time that a patient spends in healthcare settings. If oral DEC-C is approved for this indication, DEC-C plus venetoclax could represent the first all-oral induction-equivalent regimen for AML.

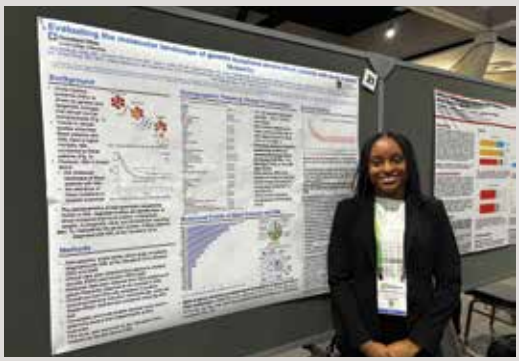
"A two-pill regimen, taken at home, eliminates the monthly 7-day clinic visits required for parenteral azacitidine administration... it is the difference between treatment that is theoretically accessible and treatment that is actually feasible..."

Taken together, these two trials pave the way for potentially transformative, randomized phase 3 studies that could use total oral therapy to challenge the standard use of parenteral IC in defined subsets of patients with newly diagnosed AML. Earlier-phase trials will examine total oral therapy approaches with triplets or even quadruplets for some patients with AML to, speculatively, functionally cure some patients without the need for IC or HCT. This may seem far-fetched today, but we have already seen similar transformative paradigm shifts in other difficult-to-treat hematologic cancers such as multiple myeloma. Leukemia doctors should start dreaming and be excited about what comes next.

Amer M. Zeidan participated in advisory boards, consulted, participated in clinical trial committees, and/or received honoraria from AbbVie, Akesobio, Agios, Amgen, Astellas, BioCryst, BeiGene, Boehringer Ingelheim, Celgene/BMS, Chiesi/Cornerstone Biopharma, Daiichi Sankyo, Dr Reddy, Epizyme, Faron, Fibrogen, GSK, GlycoMimetics, Genentech, Gilead, Geron, Janssen, Jasper, Karyopharm, Kyowa Kirin, Keros, Kura, Novartis, Notable, Orum, Otsuka, Pfizer, Regeneron, Rigel, Seattle Genetics, Shattuck Labs, Schrödinger, Syros, Syndax, Servier, Takeda, Treadwell, Taiho, Vincerx, and Zentalis.

Blood Cancers Today *spotlights the latest research from medical residents and fellows in the field of hematologic malignancies*

A Deeper Look at AML Disparities Reveals Persistent Patterns and New Unknowns



*By **Nichole Tucker***

At Cleveland Clinic Lerner College of Medicine, a medical student set out to answer a question that is rooted in biology and inequity. Under the mentorship of Anjali Advani, MD, **Eno-obong B. Udoh** sought to merge her interest in health disparities with a deepening focus on hematologic malignancies, an effort that would evolve into a retrospective cohort study examining the genetic underpinnings of acute myeloid leukemia (AML) in Black patients.

Eno-obong B. Udoh

Udoh presented the findings on behalf of her research team at the American Association for Cancer Research Annual Meeting this spring, offering a closer look at a population often underrepresented in molecular analyses of AML.

At the core of the investigation was a fundamental question: Which genetic mutations are most prevalent in Black patients with AML, and what might they reveal about persistent survival disparities? Using next-generation sequencing, Udoh and her collaborators began to dig deeper into the genetic roots of AML, mapping a molecular landscape that remains incompletely understood but increasingly central to advancing equitable care.

"The goal was to bridge our understanding of genetic drivers in AML with the reality of disparities we continue to see in Black patients," Udoh explained in an interview with *Blood Cancers Today*. "…By understanding which mutations are most common, we can begin to ask how biology may or may not be contributing to differences in survival—and how to address it," she added.

The study examined information from patients diagnosed with AML from 2002 to 2022, comprising a 1,264-patient cohort, of whom 118 (9.34%) identified as Black. Of this subgroup, 55% were male, with a median age of 62 years.

By karyotype analysis, investigators found that a significant percentage of Black patients in the cohort had an abnormal karyotype due to trisomy 8 (23.0%). Moreover, abnormalities of −7 or del (7q) were observed in 17.6% of patients, and abnormalities of −5 or del (5q) were seen in 16.2%. Among the 49.1% of patients with available next-generation sequencing data, Black patients showed a notable predominance of mutations in genes involved in DNA methylation, including *DNMT3A* and *TET2*. These two mutations were identified in 24% and 21% of patients, respectively.

Udoh explained: "Although *DNMT3A* and *TET2* were among the most frequently observed mutations, we did not find that these alterations independently informed prognosis in our cohort."

Most patients in the study received induction chemotherapy (65%), and 30% underwent bone marrow transplant. The results showed a median overall survival (OS) of 24 months (95% CI: 14-46 months). The 5-year OS rate shown was 27% (95% CI:18%-40%), which was notably lower than the national average (32.9%).

"These mutations appear to represent early events in leukemogenesis, but their prognostic significance in this population remains unclear," Udoh said.

The findings highlight both familiarity and uncertainty. While *DNMT3A* and *TET2* emerged as common mutations, mirroring broader AML data, their role in shaping outcomes in this population remains unclear. Udoh noted, "the mutations are familiar, but what they mean for this population is not, and that's the gap we have to close."

For investigators, that gap underscores the need for larger, more comprehensive studies to better define risk and, ultimately, to help close the survival disparities that persist for Black patients with AML.

"Defining the biology is only the first step—what matters next is translating that knowledge into more equitable outcomes," said Udoh.

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PHOTO CREDIT: Eno-obong B. Udoh

What Fellows Want and the Turning Point in Training

*By **Nichole Tucker***

Fellowship programs are often highly structured and carefully designed to meet the evolving demands of oncology practice. Yet, as training priorities expand, one consideration has historically received less attention: not every fellow is preparing for the same career.

For decades, oncology fellowships have reflected academic models of practice. But growing recognition is taking hold across graduate medical education.

At the Rural Oncology Conference 2026, that shift emerged as a central theme during a panel discussion on educating the next generation of oncologists. The conversation highlighted an important reality in workforce development: preparing physicians for rural oncology requires intentional training pathways.

According to **Lori Rosenstein, MD,** Hematology and Medical Oncology Fellowship Program Director of the Gundersen Health System, that model is beginning to change.

Lori Rosenstein, MD

"Just thinking about it as a legitimate career choice and deliberately training fellows to do it well is really exciting," Dr. Rosenstein said in an interview with *Blood Cancers Today*. "Historically, those interested in rural locations were left to figure it out on their own. Now we are trying to gear the training to the needs of the fellows and really help them be successful from the beginning."

The recalibration toward aligning training with career goals is gradually becoming a central theme across teaching hospitals.

For **Maura Barry, MD,** a medical oncologist and assistant professor at the Larner College of Medicine at the University of Vermont, there is a starting point that is straightforward but often overlooked: listening.

Maura Barry, MD

"One of the most important things that we can do for our fellows is really listen to what their goals are and then create a program that's tailored to their individual interests and goals for their career," Dr. Barry said in an interview. "Creating a really goal-concordant fellowship program is going to be an incredibly important part of developing a robust and appropriate workforce."

For fellows pursuing rural practice, that alignment carries specific implications.

"For oncologists practicing in rural communities, it's going to be important to have the ability to problem solve and figure out what the most realistic treatment is for a patient," Dr. Barry said. "It's an excellent grasp of guideline-based care, combined with the ability to use technology when something isn't seen as frequently."

Rural oncologists often manage a wide range of disease states without immediate access to subspecialty support, requiring the core skill of knowing when and how to reach beyond one's own clinical environment.

Dr. Rosenstein emphasized that these connections are not incidental. They must be built into training.

"The process of creating collaborative infrastructures between academic and community practices benefits both groups," she said. "Sharing tumor boards, collaborating on difficult cases, and working in partnership helps support high-quality care."

Exposure to rural settings is a key part of that process. But panelists emphasized that exposure alone is not enough. Fellows must understand both the opportunities and the constraints of rural practice.

"We want excellence to be the first goal, regardless of where someone practices," Dr. Barry noted.

The panelists perspectives reflect a broader shift in oncology education, one that recognizes rural practice as equally rigorous, complex, and essential to cancer care delivery. Yet, the larger lesson may extend beyond geography.

In a field as varied as oncology, training may be most effective when it recognizes that excellence is not tied to a single pathway, but to whether physicians are equipped to succeed wherever they choose to practice.

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Outsmarting Cancer: How Combination Therapy Is Tackling Drug Resistance

*By **Mollie Leoni, MD***

It has been 60 years since Dr. Emil Frei, known as the father of combination chemotherapy,[1,2] revolutionized the treatment of cancer when he and his colleagues at the National Cancer Institute launched the first-ever combination therapy in pediatric patients with acute leukemia.[3,4] This set off a long history of dual therapies in anti-cancer drugs, improving efficacy via targeting different pathways, compared with monotherapy.[5]

In 2007, monotherapies made up 70% of oncology drug clinical trials; in less than 15 years this fell to 20 to 30%.[6] Paired with the significant increase in overall oncology clinical trials, we now have more combination therapy clinical trials underway than ever before. Each of these trials will inform our understanding of optimal cancer regimens, with the goal of improving patients' lives. But our work isn't done–there are still swaths of patients with cancer who experience lower survival rates and desperately need improved outcomes. I strongly believe combination therapy is one way to get there.

- A challenge of chemotherapy has long been the lack of differentiation between treatment attacking cancer cells versus healthy cells. Combination approaches with precision medicines and immunotherapies have been shown to provide some protection of normal cells from the cytotoxic effects of chemotherapy.[5]
- Drug resistance remains a major barrier in cancer treatment–combination therapy may reduce these rates.[3]
- Combination therapy does have its challenges; however, getting ahead of any potential negative interactions and understanding pharmacokinetic profiles are an early priority when researching potential combination approaches.

Combination Therapy at Work

Acute myeloid leukemia (AML) provides a case study for us to understand combination therapy at work. AML is a cancer driven by many different genetic and chromosomal abnormalities that converge on a common phenotypic end point: the rapid growth of immature, nonfunctional blood cells that accumulate in the blood and bone marrow and interfere with normal hematopoiesis. Historically, AML treatment has focused on treating that common end point where the cells are already leukemic, often with chemotherapy.

However, technological advances have enabled a deeper understanding of the genetic drivers of AML and how to best treat it. The field is moving away from the "sledgehammers" of chemotherapy and toward a precision-based approach, where specific therapies are developed for genetically defined types of AML. This approach holds great promise for patients who lack therapeutic options and face poor outcomes.

The reason combination therapy can be so effective in AML is that each drug has a defined role. In combination, chemotherapy can debulk tumors and clear the way for targeted therapies to provide precise treatment, commonly known as precision medicine. This is emerging as a potential optimal therapeutic approach across different targeted therapies, and it shows how combination therapy can become a reality across disease states.

Combination approaches in AML have the potential to eliminate the need for continuous lines of therapy while maintaining the tolerability and efficacy required for long-term maintenance therapy. When I see these possibilities on the horizon, it's impossible not to be excited as a scientist and physician committed to addressing unmet patient needs.

For treatment classes such as PD-1 and PD-L1 inhibitors that can address various tumor types,[6] we see combination therapy as a key pathway to reduce drug resistance and thereby improve outcomes. CTLA-4 inhibitors, in combination with PD-1 and PD-L1 inhibitors, are approved for treatment in tumor types including melanoma, renal cell carcinoma, and hepatocellular carcinoma.[6] This combination approach has shown increased response rates and median survival time, proving in the real world how combination therapy can change the standard of care.[6]

Our field has come a long way in 60 years. Focused investment and understanding of combination therapies are laying the groundwork for treatments that have the potential to improve and extend lives across cancer types. It's an exciting time to develop combination therapeutics and address patients' needs through creative approaches.

Disclosure: Mollie Leoni, MD, is chief medical officer of Kura Oncology, which is developing therapies to be used in combination for the treatment of AML.

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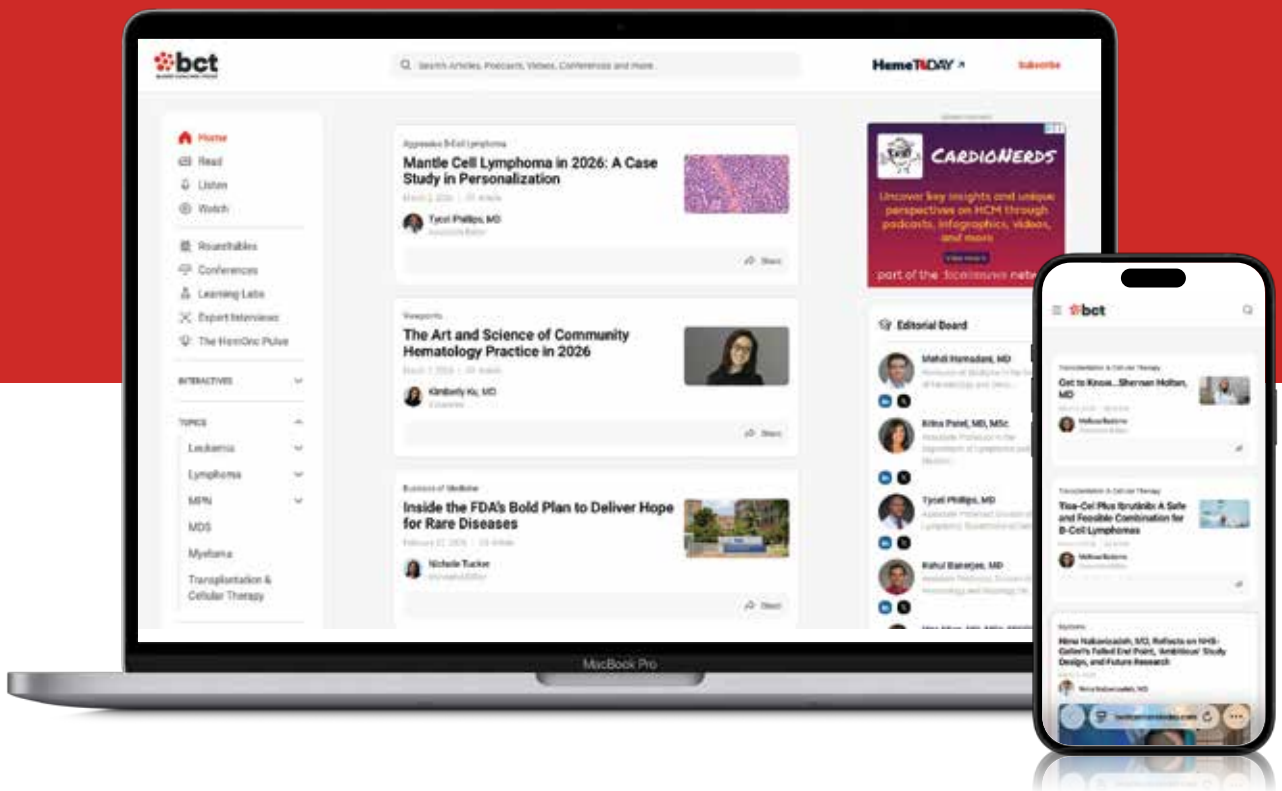

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Masashi Miyauchi, MD, PhD

At Stanford Medicine in California, hematologist-oncologist Masashi Miyauchi, MD, PhD, uses stem cell technology to develop cancer models and hematopoietic stem cell expansion systems to improve outcomes for patients with blood cancers.

*By **Melissa Badamo***

Originally from Japan, Dr. Miyauchi received his Doctor of Medicine from Kyoto University and his Doctor of Philosophy from the University of Tokyo. Drawn to science and biology at a young age, Dr. Miyauchi credits the popular 1970s Japanese manga *Black Jack*—which centers around a heroic surgeon—as his inspiration for pursuing medicine.

"That was my fundamental motivation. I wanted to help people who suffer from a disease, just like the surgeon in that comic," he said. "During my university student days, I was fascinated by biological and scientific topics such as immunology, neurology, and DNA repair. I pursued hematology because it is a nice mixture of stem cell biology and immunology. As for oncology, it is very easy to understand the outcomes. When I do oncology research, the outcomes may be that the counts are decreased or the survival is longer. The readout is clear."

"There are two ways to utilize stem cell technology to improve patient outcomes. The first is to develop a new disease model, and the second is to directly utilize the stem cell for cancer treatment."

After medical school, Dr. Miyauchi pursued a senior residency in internal medicine and a clinical fellowship in hematology and oncology at the University of Tokyo Hospital, where he was involved in the clinical care of patients with blood cancers through hematopoietic stem cell transplantation (HSCT). This experience laid the path for his postdoctoral journey at the Nakauchi lab at Stanford University, where he studies cancer patient–specific induced pluripotent stem cells (iPSCs).

"Ideally, we can generate any type of tissue or cell from iPSCs," Dr. Miyauchi said. "That is very fascinating technology. The goal is to make a new disease model to dissect the mechanism of the disease."

In 2018, Dr. Miyauchi and colleagues successfully developed a humanized mouse model for chronic myelomonocytic leukemia (CMML) derived from iPSCs from a patient with CMML.[1] Next, Dr. Miyauchi will focus on developing models for other blood cancers as well as validating the feasibility of this mechanism through gene editing.

"We are now developing myelofibrosis iPSCs," he added. "We can utilize that platform to dissect a new mechanism, which would ultimately help investigate new therapeutic targets for myelofibrosis."

The second area of Dr. Miyauchi's research focuses on expansion of human hematopoietic stem cells in vitro to overcome current limitations of HSCT.

"One limitation of HSCT—which is a useful treatment option for multiple types of cancer—is that we can obtain the blood stem cell from a healthy donor, but we cannot maintain or even expand that human stem cell," he explained.

At the 67th American Society of Hematology Annual Meeting, Dr. Miyauchi presented findings from a long-term expansion protocol for human hematopoietic stem cells. He found that supplementing FLT3 ligand with lusutrombopag and stem cell factor enhanced ex vivo expansion and maintenance of phenotypic hematopoietic stem cells from CD34 + umbilical cord blood cells.[2]

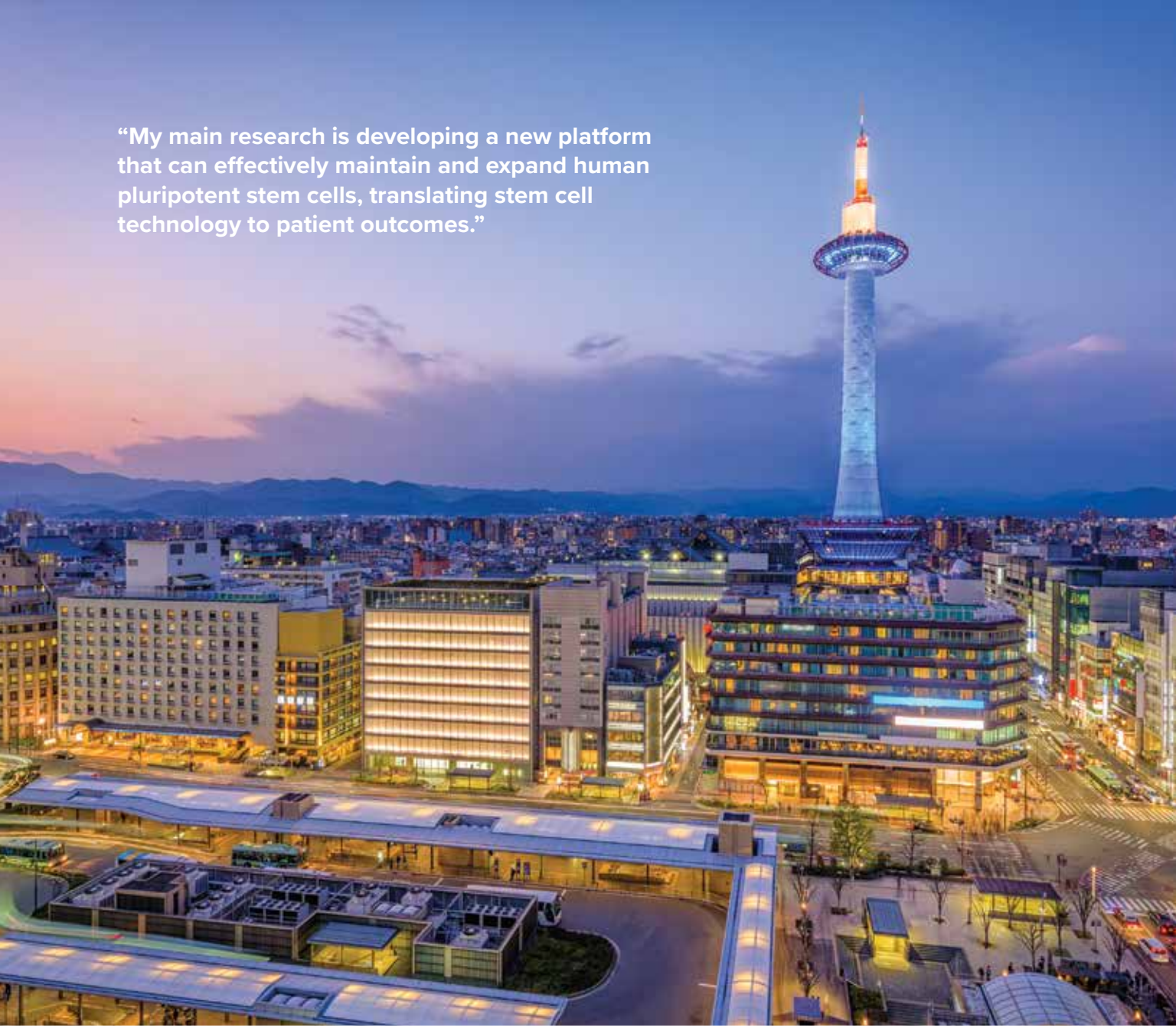

PHOTO CREDIT: ISTOCK.COM/SEAN PAVONE

“There are two ways to utilize stem cell technology to improve patient outcomes. The first is to develop a new disease model, and the second is to directly utilize the stem cell for cancer treatment,” Dr. Miyauchi summarized. “My main research is developing a new platform that can effectively maintain and expand human pluripotent stem cells, translating stem cell technology to patient outcomes.”

Outside of research, Dr. Miyauchi enjoys spending time with his two children—aged 6 and 10—and accompanies them to after-school activities such as karate, ballet, and soccer.

“Soccer is not popular in Japan, but here it is a very popular activity. Because I was born and raised in Japan, watching them play soccer is a way for me to experience my children’s lives in the United States,” he said. “My kids also like to read comics in Japanese and English. We push them to read in both languages to maintain their Japanese.”

Similarly, Dr. Miyauchi encourages his children to pursue a career path that helps people—whether it be a teacher, lawyer, or doctor. He is also involved in educating high school and university students in Japan through web-based programs.

“I’m fascinated about the education for the younger generation,” he said, offering advice for younger trainees in the hematology oncology field. “The hematology oncology field is a nice mixture of basic biology and translational research. If a trainee were to pursue hematology oncology, the field will stimulate their interest. I would encourage them to follow their choice.”

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Precision Diagnostics:

Continued Incremental Integration Into Hematologic Malignancy Management

By ***Leah Lawrence***

One of the earliest examples of the potential of precision diagnostics comes from hematologic malignancies and the development of imatinib for chronic myeloid leukemia (CML).[1] Now, more than 25 years later, discoveries in precision diagnostics continue to advance the field.

"We like to think of precision medicine and precision diagnostics as ways to treat each individual patient more specifically," said **Justin M. Balko, PharmD, PhD,** a professor of medicine in the Division of Hematology and Oncology, Department of Medicine, at Vanderbilt University Medical Center. "A ton of work in the last 40 to 50 years has been centered in the era of evidence-based medicine and large randomized controlled trials where we attempt to define a disease type with certain molecular or pathologic features. It has been centered on finding ways to treat smaller and better-defined patient populations rather than treating large patient populations all in the same way."

The knowledge gained has been applied to disease management in various ways, including determining prognosis, selecting appropriate treatments, or tracking response.

Next-Generation Sequencing

The use of next-generation sequencing (NGS) varies in importance and timing depending on the type of hematologic malignancy. In the example of CML, NGS at diagnosis can identify the hallmark *BCR:ABL1* fusion gene. Similarly, in acute myeloid leukemia (AML), NGS can identify genetic abnormalities that dictate the use of targeted therapies such as *FLT3, NPM1, IDH1* and *IDH2*, and more.[2,3] In recent years, the FDA has approved therapies for patients with these mutations. These include ivosidenib, enasidenib, and olutasidenib for *IDH1* or *IDH2* gene mutations, quizartinib, gilteritinib, and midostaurin for *FLT3* mutations, menin inhibitors revumenib and ziftomenib for KMT2A translocations and *NPM1* mutations.[4,5]

"However, every blood cancer is different," said **Manni Mohyuddin, MD,** an assistant professor in the multiple myeloma program at the Huntsman Cancer Institute at the University of Utah in Salt Lake City. "In AML, you have a genetic abnormality that may dictate what sort of treatment we do, but in myeloma, that is definitely less the case."

Multiple myeloma, he said, is a bit further behind with no specific treatments given based on what genetic abnormalities a patient's cancer has. "Part of this is that we are fortunate that our treatments, on average, work well for most people and work for a long period of time," he said.

Similarly, according to **Natalie S. Grover, MD,** associate professor in the division of hematology at University of North Carolina School of Medicine, NGS is not used to determine targeted therapies for lymphomas.

"I don't use it much in my daily practice for treatment decisions," Dr. Grover said. "However, there are some mutations that provide prognostic information."

For example, patients with *TP53* mutations are thought to have a worse prognosis and are not as sensitive to chemotherapy, Dr. Grover said. Unfortunately, detection of *TP53* through NGS can be costly and time-consuming.[6,7]

"That is one of the challenges with precision medicine," Dr. Balko said. "Clinicians have to know that this technology, these tests, will not only help them to know what to do or change for their patients, but that these changes will influence patient outcomes. That is often hard to prove."

Within chronic lymphocytic leukemia (CLL), the main molecular tests include *IGHV* gene mutation analysis and NGS for *TP53* mutations, according to **Michael Choi, MD**, HS clinical professor of medicine at the University of California, San Diego Medical Center.

"In my practice, *IGHV* testing is routine," Dr. Choi said. "I find that this helps provide a general sense of prognosis for patients and can help guide things like frequency of initial visits and can be one of the factors to consider in treatment decisions."

That said, the current main treatment options for CLL—BTK inhibitors and BCL2 inhibitor-based treatment—are still effective in cases with *TP53* mutations or unmutated *IGHV*, Dr. Choi said, "but the duration of remission may not be as long with fixed-duration treatment strategies."

Liquid Biopsy

Complementary to NGS, liquid biopsy and measurable residual disease (MRD) monitoring have also improved risk stratification and therapeutic decision-making for certain hematologic malignancies.

In acute lymphoblastic leukemia (ALL), MRD has been part of a patient's risk stratification for years, but has more recently become part of therapeutic decision-making for these patients. For example, data have shown that patients with standard-risk ALL who achieved deep MRD negativity can forego hematopoietic stem cell transplant (HSCT). For patients who have undergone HSCT, a rising MRD level can indicate disease relapse and prompt initiation of salvage therapy. Finally, patients who do not respond to frontline therapy and remain MRD positive can receive subsequent MRD-directed treatments.[8]

In CML, MRD monitoring can help clinicians identify patients who are responding well to treatment and may be eligible for treatment discontinuation, or those at risk of resistance who need to switch treatment regimens.[9]

For CLL, Adaptive's clonoSEQ or similar assays can be used to assess for MRD after treatment, Dr. Choi said, with the information used to help determine if a patient can safely stop taking fixed-duration therapies or to detect early signs of relapse. This test has high sensitivity, especially in clinical trials, but baseline samples are needed to track MRD.

"While it is available to be done outside of trials, it can take some foresight to have a baseline sample sent for analysis," Dr. Choi clarified.

Within multiple myeloma, MRD status is known to be prognostic, and MRD-directed therapies are being studied within clinical trials. These trials are exploring strategies related to de-escalation or intensification of therapy based on a patient's MRD status, Dr. Mohyuddin said.

"I would love to see bold trials where we evaluate if people with standard-risk myeloma who respond well to treatment can really truncate the duration of treatment," Dr. Mohyuddin said. "Currently, everybody still gets several years of treatment before a MRD-guided de-escalation can happen. Can we cut that down?"

In lymphoma, liquid biopsy is slowly making its way into the clinic, but it is not used universally, Dr. Grover said.

"We often use PET scans to monitor for residual disease, but we know that we can sometimes get false positives," Dr. Grover said. "You can't always biopsy a patient to confirm residual disease. In those cases, I like to get circulating tumor DNA to complement the PET."

A negative ctDNA test is reassuring, Dr. Grover said. "On the flip side, if the ctDNA test is positive, it tells me to potentially start thinking about the next therapy or to initiate therapy."

Other Considerations

Ultimately, the goal of precision medicine is for every patient to receive the specific treatment that is most beneficial to them. Progress toward that goal must be grounded in evidence-based research, and that takes time and can be fraught with barriers, Dr. Balko said.

For example, historically, research into the use of MRD for multiple myeloma and standardization of its measurement faced challenges, Dr. Mohyuddin said.

"The word 'MRD' was being thrown around a lot with assays of all types and sensitivity, with many different methodologies being used," Dr. Mohyuddin said. In 2022, Dr. Mohyuddin and colleagues published data showing the heterogeneity of MRD methodology and sensitivity across multiple myeloma clinical trials conducted from 2015 to 2020.[10]

However, since then, the field has worked to standardize definitions and reporting of MRD, and there are now widely accepted guidelines on how MRD data should be measured and reported.

"Most recent myeloma trials are using Adaptive, which has an MRD assay with a sensitivity of 10^{-6}," Dr. Mohyuddin said. "It is a challenge, but the field has done a good job of harmonizing."

In AML, the European LeukemiaNet has updated its guidelines to provide a comprehensive framework for MRD assessment that is aligned with its genetic risk classification. Any attempt at widespread implementation of these precision approaches will require this type of standardization.

Issues related to cost, turnaround time, and access also exist.

"Turnaround time is an issue, particularly for these tests that are very patient specific," Dr. Balko said. "These advanced, ultrasensitive MRD assays are detecting very specific DNA copies at very, very low frequency and it takes significant time to create these patient-specific assays."

As more applications in clinical practice develop, faster turnaround times will be important. Increased applications will also likely lead to more widespread access.

"Historically, these technologies were only used at academic centers, but there has been a lot of buy-in now from the community," Dr. Mohyuddin said, addressing the use of MRD for multiple myeloma. "Adaptive is now being run at more than 1,000 sites in the US. Clearly, the field is recognizing that this technology is at the point where it can help make decisions."

Dr. Mohyuddin said there are still some glaring areas where these tests are not widely used or readily available, such as within Veterans Affairs and in more rural areas, but added that he is very optimistic this will change over time.

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Off the Map: Vanishing Routes Isolating Rural Hematologic Oncology Care

By ***Nichole Tucker***

Rural hematology/oncology clinicians are navigating growing logistical and clinical challenges as the care infrastructure continues to narrow, with cancer care pathways becoming harder to follow and less reliably connected. Across the United States, 146 rural hospitals have closed since 2005, and more than 400 remain at risk as of 2026.[1-3] In parallel, chemotherapy services have also declined, further eroding key access points and adding strain to care coordination, treatment delivery, and toxicity management in rural communities.

As these closures redraw the landscape, the familiar routes patients once relied on for cancer care are disappearing. While clinicians work to navigate these impeding setbacks, the downstream impact on patients is even more profound. It extends beyond care delivery to fundamental issues with access, leaving many communities increasingly off the map when it comes to consistent, coordinated oncology care.

PHOTO CREDIT: ISTOCK.COM/TOE DESIGN

When Continuity Breaks Down

Rural hospital closures disrupt local health infrastructure by weakening continuity of care, which starts with removing critical points of access to care. This was first underscored in a 2022 report from the American Hospital Association.[3] Recent research has amplified the concern, showing that closures reduce the availability of healthcare professionals and degrade ongoing management of acute and chronic illnesses.[4]

Specifically, the research underscores that residents of rural communities experience longer transport times for emergency care and face fragmented care pathways when hospitals close their doors. As local access points disappear, patients are no longer guided along a coordinated system of care. Instead, patients must navigate between multiple distant facilities on their own. This leads them to seek services across disconnected locations rather than through a clear, unified care route.

The downstream impact of rural hospital closures began more than 10 years ago. Between 2014 and 2024, 228 rural hospitals stopped offering chemotherapy services, representing a 22% reduction across the US. Some states have been impacted more than others; for example, more than half of rural chemotherapy services in Mississippi have disappeared.[1] This decline in local oncology care forces patients to travel longer distances to receive treatment. This can be especially challenging for older adults and low-income patients, as well as those with physical disabilities.

These access challenges are further complicated because rural barriers are not limited to distance or hospital availability alone. They are reinforced by transportation instability, geographic isolation, workforce shortages, and environmental constraints that can make sustained cancer care difficult even when services technically exist nearby.

As **Manali Patel, MD,** of Stanford Medicine, highlighted in an interview, "The most commonly cited issues are transportation, which compounds barriers to care. Rural patients are reliant on transportation, and public transportation options are lacking. Now with the rising cost of fuel, this financial impact can further worsen care receipt. In addition, there are distinct challenges faced by patients who live in these areas, and many of these challenges can be unique to the area. For example, seasonal inaccessibility of roads in some areas with rugged terrain poses barriers that can deplete access to healthcare infrastructure."

Dr. Patel continued: "Furthermore, the limited workforce network in these settings can compound these concerns. Given that many of these areas have limited healthcare workforce, the vulnerability of the network is limited—the departure of a single physician or ancillary staff member can disrupt care for many in those areas and severely disrupt the care network for people. Cancer care is multidisciplinary and requires access to many different types of physicians. Therefore, it is especially susceptible to these disruptions."

In providing care to patients with hematologic cancers, more considerations come into play. In an interview, **Jonathon B. Cohen, MD, MS,** of Winship Cancer Institute at Emory University, explained the implications for treatment. "As we are continuing to make great strides in care for patients with cancer, it is increasingly clear that patients will need access to excellent care in a location that is surrounded by their community. This requires not only oncologists with appropriate training, but also the infrastructure to implement increasingly complex therapies. When oncology centers are forced to curtail services, this can result in patients either not having access to the standard-of-care treatments or require them to travel further away, at a distance from their community. This does have a direct impact on the likelihood of a patient being cured."

Cellular therapies also play a large role in the treatment of hematologic malignancies, and although treatments like chimeric antigen receptor T-cell therapy and stem cell transplantation are carried out at tertiary centers, referrals to such services are handled locally.

"As we are continuing to make great strides in care for patients with cancer, it is increasingly clear that patients will need access to excellent care in a location that is surrounded by their community."

—Jonathon B. Cohen, MD, MS, Winship Cancer Institute at Emory University

"Patients in rural communities rely on their local healthcare system for supportive care before and after receiving these treatments. When hospitals and clinics close, it requires patients to stay closer to the tertiary care center for longer, which can be expensive and also keep them away from their loved ones and support system," said Dr. Cohen.

In an interview, **Bhavana (Tina) Bhatnagar, DO,** of WVU Medicine, the medical center of the University of West Virgina in Morgantown, explained: "Further downstream effects will be realized over time as treatment delays impact disease stage. There's significant anxiety and stress that rural oncology patients endure when they finally are able to be seen and evaluated for their cancer diagnosis. A cancer diagnosis, in and of itself, is a life-changing event for patients and their families."

Access alone is not the only barrier. Financial factors and reimbursement challenges in low-volume settings have also impacted rural facilities.

The Financial Ripple of Closures

Financial instability is central to the ongoing wave of rural hospital closures, driven by a combination of persistent operating losses, inadequate reimbursement, and limited financial reserves. According to a report from the Center for Healthcare Quality and Payment Reform, hundreds of rural hospitals are operating at a loss.[2]

In an interview, **Brock Slabach** of the National Rural Health Association said, "Where we see the risk factors for hospitals in terms of their operations, we have low revenue growth, meaning they're not expanding services operating performance. In terms of margin, 40% are operating in the negative capacity."

Adding to the dilemma, many rural hospitals rely on supplemental funding sources, such as local taxes or state subsidies, to offset deficits, but these revenue streams are not stable; they are not guaranteed over the long term. The high risk of closure for rural hospitals makes clear how structural payment inadequacies and thin financial margins continue to threaten health systems. Issues with insurance reimbursement are also relevant.

Slabach explained that Medicare Advantage plans remove patients from traditional Medicare guarantees, including critical access hospital provisions and low-volume hospital programs. This reduces predictable revenue streams for rural facilities. The financial pressure can limit the ability of rural hospitals to maintain costly oncology services or invest in new care delivery models.

Slabach continued: "We are looking at how we can maybe change the payment structure so that we can incentivize different behavior—one that rewards innovation around chronic disease management, around the nature of moving into the community in terms of service outside of the four walls of the hospital or clinic. Secondly, we are looking to see how these payment structures can be organized, these innovation programs can be organized, so that they don't put the hospital or clinic financially at risk because they are putting themselves out of business through saving other people or other entities money," said Slabach. "So, we need to find a way to keep those savings local. And of course, one of those programs has been, historically, the Medicare Shared Savings Program, or MSSP, that many hospitals in rural areas have participated in, which has provided a significant amount of savings that they've been able to use and plow back into their programming at the local level."

Regarding reimbursement, Slabach explained that there is work to be done that may help over time. "If closures continue at the current pace, attending to reimbursement will be critical—particularly designing payment programs that incentivize the outcomes we want to see in rural communities."

The financial strain is not merely impacting healthcare companies, but also patients. According to Dr. Cohen, financial toxicity among patients is imminent in this case. "This is particularly problematic in communities located far from the large centers. If a patient needs to have repeated visits to a large center, it often requires not only their time but the time of a caregiver to take them and provide support. This can result in patients missing work, accessing childcare, increased cost to the patient and caregiver, and a number of downstream impacts. … For caregivers, who may be caring for several family members, this can create large amounts of stress and hardship," he said.

More financial considerations are upcoming for rural hospitals, such as One Big Beautiful Bill, H.R.1, which divides funds for hospitals among all US states. However, there are advocacy efforts under way to help slow down the closures by organizations such as the National Rural Health Association. Moreover, experts in hematologic oncology believe more work in healthcare systems can be done to minimize the impact on patients with cancer.

Stabilizing Rural Hospitals Now and Ahead

Looking ahead, the trajectory of rural hospital stability will depend heavily on whether payment reform and targeted investments can keep pace with impeding financial pressures. "We're going to be watching the next 5 years closely as states implement the Rural Health Transformation Program to see if any bright spots emerge that can be scaled as best practices," Slabach said.

Healthcare models will be more important than ever. For example, share-care programs, telemedicine, and satellite infusion centers are needed.

Supporting this shift toward more decentralized and accessible models of care, Dr. Patel noted the growing role of telehealth and hybrid care delivery systems in reducing rural access barriers, stating, "Certainly one of the most widely studied interventions is telehealth and virtual care models."

"We are working on each of these [telehealth and virtual care] to try to improve access to care, even for patients located outside of our primary site," Dr. Cohen explained. "Patients repeatedly request the ability to receive care closer to home, and we've been able to accomplish this. It alleviates much of the stress and anxiety and often allows the patient to focus more on their disease and treatment rather than the logistics of attending appointments. I would love to see this expand further. Currently, there are challenges with implementing clinical trials in the rural setting, and I am hopeful that with investment from industry, collaboration with tertiary care sites, and some decrease of the regulatory burden on sites to conduct trials, we can make this happen."

The issue of rural hospital stability also calls for more investment in the patients themselves, as Dr. Bhatnagar explained during the interview. "With the closure of rural hospitals, I think it will be important for the remaining hospitals that provide oncology care to properly absorb these patients and ensure there is a streamlined process for patients in rural areas to receive proper care. I think those discussions need to happen before a rural hospital is slated to close. More widespread adoption of telemedicine services may be one way to alleviate the influx of patients, or perhaps a dedication of time, space, resources, and facilities to a rural oncology clinic, under the umbrella of a tertiary care center, to provide such patients with the care they deserve."

"There's significant anxiety and stress that rural oncology patients endure when they finally are able to be seen and evaluated for their cancer diagnosis. A cancer diagnosis, in and of itself, is a life-changing event for patients and their families."

—Bhavana (Tina) Bhatnagar, DO, WVU Medicine

Ultimately, the path forward will require industry stakeholders to rethink how care is financed so that innovation is meaningfully supported. Payment models must evolve in a way that not only encourages new approaches to care, but also helps redraw a more sustainable map for rural oncology—one where access points remain connected rather than fading into isolation. This ensures that efforts to generate savings do not occur at the expense of the very systems that patients rely on to navigate their care.

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Regulatory Actions

Regulatory approvals, designations, and guidance in the field of hematologic oncology

Scan to learn more.

April 30, 2026

Selinexor Withdrawn From FDA Accelerated Approval for DLBCL

The FDA has withdrawn accelerated approval of selinexor for relapsed or refractory diffuse large B-cell lymphoma (DLBCL) due to an incomplete phase 3 study. The XPO1 inhibitor initially received accelerated approval in June 2020 for the treatment of adult patients who had received at least two lines of prior therapy.

May 1, 2026

FDA Approves Ruxolitinib Extended-Release Tablets for Myelofibrosis, Polycythemia Vera, and GVHD

Ruxolitinib extended-release tablets have been FDA approved for the treatment of adult patients with myelofibrosis, adult patients with polycythemia vera, and adult and pediatric patients 12 years or older with graft-vs-host disease (GVHD). Developed by Incyte, the tablets are branded under the name Jakafi XR and provide an extended-release, once-daily version of ruxolitinib.

May 3, 2026

Axatilimab Approved in Australia for Chronic GVHD

Australia's Therapeutic Goods Administration has approved axatilimab, a first-in-class novel colony-stimulating factor-1 receptor-blocking antibody, for patients with chronic GVHD. Axatilimab was approved in the US in August 2024.

May 4, 2026

FDA Clears Investigational New Drug Application for Phase 1b/2a Trial of CK0802 in Steroid-Refractory GVHD

After FDA clearance of an Investigational New Drug Application, Cellenkos, Inc. will begin a phase 1b/2a clinical trial of CK0802, a first-in-class regulatory T-cell therapy, for patients with steroid-refractory GVHD. With an anticipated start date of mid-2026, the study will evaluate safety and early efficacy assessed by overall response rate.

Highlights from the **2026 AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING,** May 29–June 2, 2026, in Chicago, Illinois

ERASMM Study Suggests Elranatamab May Improve Outcomes in High-Risk Smoldering Myeloma

*By **Nichole Tucker***


Cyrille Touzeau, MD, PhD

Initial efficacy and safety results from the phase 2 ERASMM study of elranatamab for high-risk smoldering multiple myeloma (HR-SMM) have been presented at the American Society of Clinical Oncology Annual Meeting. According to the lead study investigator, **Cyrille Touzeau, MD, PhD,** professor of hematology at the University Hospital of Nantes in Nantes, France, this study was launched in an effort to improve outcomes shown with standard treatment approaches for patients with HR-SMM.

"With lenalidomide or daratumumab in HR-SMM, rate of deep response is very low. The BCMAxCD3 bispecific antibody elranatamab demonstrated strong anti-myeloma activity, with a favorable safety profile in relapsed MM. Using T-cell engagers in the early stage of the disease, with less altered immune system, we hypothesized improved efficacy with potentially reduced risk of infection," Dr. Touzeau told *Blood Cancers Today*.

To investigate the promise of elranatamab, the ERASMM study enrolled 50 patients with previously untreated disease from 17 centers globally. Those enrolled received fixed-duration elranatamab starting at 12 mg and 32 mg, followed by 76 mg administered on a specific day during the cycle. Early findings suggest the dosing approach translated into meaningful clinical activity while maintaining manageable toxicity.

"With a median follow up of 14 months, most patients achieved CR [complete response]. Among them, more than 90% of evaluable patients achieved undetectable (10^{-6}) MRD [measurable residual disease] negativity. Overall, safety profile was consistent with elranatamab used in the relapsed setting," Dr. Touzeau explained.

The treatment responses observed with elranatamab were deep, with nearly all patients in the study achieving measurable responses and a substantial proportion reaching very good partial responses or complete responses. In the early follow-up period, progression-free survival remained high at 9 months, and no deaths were reported at the time of analysis, demonstrating elranatamab's disease-control capabilities. As Dr. Touzeau alluded to, beyond the depth of response, safety findings shaped the overall profile of the regimen.

Elranatamab was manageable in these patients, and its safety profile appeared consistent with that of other T-cell-engaging therapies. Cytokine release syndrome was frequently observed but was predominantly low grade, and investigators reported no immune effector cell-associated neurotoxicity syndrome (ICANS) events. Infections represented a meaningful toxicity signal, with some severe cases observed. Other commonly reported adverse events included dermatologic, gastrointestinal, hepatic, neurologic, and fatigue-related effects, most of which were mild to moderate in severity. A small number of patients discontinued treatment because of adverse events, including infection-related complications and isolated serious toxicities.

These findings add nuance to the early clinical experience and help frame how the regimen may be viewed going forward, according to Dr. Touzeau.

"Of course, a longer follow-up is needed, but we think this is a very good signal to support phase 3 studies evaluating bispecific antibodies in this population in HR-SMM," he said.

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Touzea C, et al. 2026 American Society of Clinical Oncology Annual Meeting. Abstract 7500.

Real-World Data Illustrate Effect of AFib on Cardiovascular Outcomes and Healthcare Use in CLL

*By **Andrew Moreno***


Michael Fradley, MD

To what degree in patients with newly diagnosed chronic lymphocytic leukemia (CLL) does atrial fibrillation (AFib) influence cardiovascular (CV) outcomes and use of healthcare resources? A retrospective observational study led by **Michael Fradley, MD,** of the University of Pennsylvania School of Medicine in Philadelphia, engaged real-world data to answer these questions.

According to study results presented at the 2026 American Society of Clinical Oncology Annual Meeting, AFib has a pronounced effect on this patient population.

"Findings highlight significant real-world CV and HCRU [healthcare resource utilization] burden incurred by CLL patients with AFib," wrote Dr. Fradley and colleagues.

Delving into the US Symphony patient database, the investigators examined records of 233,362 adults with newly diagnosed CLL who were followed for 1 year after diagnosis to assess AFib presence. Applying multivariate regression analyses, the investigators compared CV outcomes and HCRU between patients with and without AFib.

All CV event types measured by the investigators were significantly more frequent in CLL patients with AFib than in those without. The incidences of bleeding, heart failure, and stroke in patients with AFib were 27.9%, 54.5%, and 14.3%, respectively, and in patients without AFib were 19.1%, 18.9%, and 8.9%, respectively ($P<0.001$). Along with the association of AFib with these CV events, the investigators found patient age of 65 years and older, male sex, and non-White race to carry such an increased risk for CV events ($P<0.01$).

Regarding use of healthcare services, analysis found that among patients with AFib the proportion of patients who had at least one inpatient visit within 1 year of CLL diagnosis was 54.9% as compared with 23.2% in patients without AFib ($P<0.001$). Patients with AFib were also more likely to require inpatient service, at an odds ratio (OR) of 2.28 ($P<0.001$).

The investigators also performed exploratory analyses comparing first-line interventions with the Bruton tyrosine kinase inhibitors (BTKis) acalabrutinib, ibrutinib, or zanubrutinib, and, among these three, the data indicated that zanubrutinib was most effective at reducing AFib. Within 1 year of treatment, the rate of AFib in patients who received zanubrutinib was 11% as compared with 13% in acalabrutinib recipients and 16% in ibrutinib recipients ($P<0.001$). The incidences of bleeding, heart failure, or stroke were also all lower among zanubrutinib recipients than among recipients of either acalabrutinib or ibrutinib.

First-line zanubrutinib was also associated with reduced use of inpatient services within 1 year of treatment compared with the other two BTKis. In their multivariate regression analysis, the investigators determined that, compared with zanubrutinib, the odds of inpatient service within 1 year of treatment initiation were 29% higher with acalabrutinib (OR 1.29; $P=0.005$) and 69% higher with ibrutinib (OR 1.69; $P<0.001$).

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Real-World Liso-Cel Outcomes Exceed Clinical Trial Data in Relapsed or Refractory CLL

*By **Melissa Badamo***

Emily Tomasulo, DO

The TRANSCEND CLL 004 trial established lisocabtagene maraleucel (liso-cel) as a powerhouse chimeric antigen receptor T-cell therapy for the treatment of relapsed or refractory chronic lymphocytic leukemia (CLL), leading to FDA approval in March 2024.[1] Now, an observational US study found that real-world response rates reached higher than those seen in clinical trials.[2]

The Center for International Blood and Marrow Transplant Research registry study was presented by **Emily Tomasulo, DO,** of the University of Pennsylvania, at the 2026 American Society of Clinical Oncology Annual Meeting. Dr. Tomasulo and colleagues analyzed data from 45 patients (median age, 62 years) with an Eastern Cooperative Oncology Group Performance Status of 1-2 and a median of six prior lines of therapy. Most (91%) patients had unmutated *IGHV*.[2]

At a median follow-up of 6 months, liso-cel achieved an overall response rate of 84% with a complete response (CR) rate of 55%,[2] higher than the 20% CR rate reported in the original phase 1/2 TRANSCEND CLL 004 trial.[1] While the median duration of response (DOR), progression-free survival (PFS), and overall survival (OS) were not reached in the observational study, the 6-month DOR, PFS, and OS were 89%, 77%, and 87%, respectively, among the 36 patients who responded to treatment.[2]

Among those who achieved CR, the rate of measurable residual disease (MRD) negativity was 81%.[2] In comparison, the TRANSCEND CLL 004 trial reported higher MRD negativity rates of 100% in the blood and 92.3% in the bone marrow among patients who achieved a CR.[1]

Consistent with the TRANSCEND CLL 004 trial,[1] 80% of patients experienced cytokine release syndrome (CRS), including 4% with grade 3 or higher CRS.[2] Immune effector cell–associated neurotoxicity syndrome (ICANS) occurred in 36% of patients, including 13% with grade 3 or higher ICANS. Five deaths occurred due to infection or relapse/progression of CLL. Forty percent of patients experienced infections, and 18% had grade 4 thrombocytopenia or neutropenia 30 days after liso-cel infusion.[2]

"These real-world data support liso-cel as an effective option for pts with R/R CLL, including heavily pretreated or high-risk pts, and the potential for outpatient administration," Dr. Tomasulo and colleagues concluded.[2]

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2. Tomasulo E, et al. 2026 American Society of Clinical Oncology Annual Meeting. Abstract 7024.

News Roundup

The latest news and updates in hematologic oncology research

AMA Data Show That Physicians Are Under the Threat of Lawsuits

*By **Lauren Evoy Davis***

A new report from the American Medical Association (AMA) reveals that while medical liability remains a looming shadow over the profession, lawsuits are rarely indicators of actual medical error.

Bobby Mukkamala, MD

AMA President **Bobby Mukkamala, MD,** noted that while physicians often take on high-risk cases to save lives, the constant threat of litigation drives up healthcare costs and encourages "defensive medicine."

"Doctors continue to take on complex, high-risk care because patients depend on it," he added. However, the ongoing liability risk not only challenges physicians but it increases practice expenses, reinforces defensive medical practices, and drives up healthcare costs for patients and families."

Who Is Most at Risk?

The likelihood of facing a claim varies based on age, gender, and specialty:

- The Age Factor: Experience brings risk. Physicians 55 and older (45.2%) are sued more often than physicians younger than 45 years (11%).
- High-Stakes Specialties: Obstetricians and gynecologists (59.6%) and general surgeons (53.1%) are the most likely to face at least one career lawsuit.
- The Gender Gap: Male physicians (35.1%) are sued more often than female physicians (20.6%), though researchers attribute this largely to male doctors having more years in practice on average.

The Surprising Reality of Case Outcomes

Despite the high frequency of filings, most claims do not result in a finding of fault:

- Dropped Cases: From 2016 to 2018, 65% of claims were dropped, dismissed, or withdrawn before ever reaching a verdict.
- Trial Success: When cases do go to trial, physicians win an overwhelming 89% of the time.

There is a downward trend in litigation. In 2024, 28.7% of physicians reported having been sued during their careers, a drop from 34% in 2016.

A second AMA report studied annual changes in medical liability insurance premiums from 2016 to 2025. Eleven states had at least one premium grow by 10 dollars or more in 2025. Five of these states—Pennsylvania, Kentucky, Florida, Illinois, and New York—experienced large premium increases in both 2024 and 2025.

The AMA says it wants to protect patients and urges that those who are injured while seeking medical care should be compensated fairly. The health organization aims to reduce the growth of healthcare costs while preserving access to high-quality care.

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NAMPT Inhibition: Trial Exploration Continues on a New Treatment Mechanism for AML and MDS

*By **Andrew Moreno***

A presentation at the 2026 American Association for Cancer Research (AACR) Annual Meeting provided new updates on an ongoing, phase 1 clinical trial of RPT1G for relapsed or refractory acute myeloid leukemia (AML) and higher-risk myelodysplastic syndromes (MDS) or neoplasms.[1]

RPT1G is a first-in-class nicotinamide phosphoribosyltransferase (NAMPT) hyperbolic inhibitor. In written remarks forwarded to *Blood Cancers Today,* trial team member **Aaron Goldberg, MD, PhD,** a hematologic oncologist and leukemia expert at Memorial Sloan Kettering Cancer Center (MSK) in New York City, described RPT1G's significance as the first agent with this mechanism of action to be well tolerated.

Aaron Goldberg, MD, PhD

"While NAMPT has long been recognized as an important therapeutic target in oncology, earlier attempts to inhibit the enzyme were limited by toxicity to healthy cells. RPT1G's novel hyperbolic inhibition mechanism is designed to overcome this challenge by reducing NAMPT activity to a level that kills cancer cells while

maintaining sufficient NAMPT activity to preserve normal cellular function," Dr. Goldberg clarified.

RPT1G has already shown favorable safety and tolerability in a prior phase 1 study, which assessed the agent at a single dose level and at several ascending dosages.[2] There were no agent-associated serious adverse events or any treatment-emergent adverse events (TEAEs) worse than grade 2 severity, nor did any patients discontinue therapy due to TEAEs.

"Following the successful completion of the phase 1 study in healthy volunteers, and building on the momentum of an Orphan Drug Designation from the FDA, RPT1G has now advanced into a phase 1 dose escalation study in patients with relapsed or refractory AML and higher-risk MDS." Dr. Goldberg elaborated.

That trial[3] is an open-label, multicenter study in which patients will receive oral RPT1G twice daily for 28-day cycles, starting from a dose of 120 mg and then escalating. The safety and tolerability of RPT1G will once again be evaluated, but insights will also be sought on pharmacokinetics and clinical efficacy. Researchers will also aim to establish the recommended phase 2 dose, optimal dosing schedule, maximum tolerated dose, and biologically effective dose.[1]

"The study has been enrolling patients at MSK and MDACC [MD Anderson Cancer Center], two of the foremost leukemia centers in the US, with other top leukemia sites expected to join soon. We are looking forward to evaluating RPT1G in these two patient populations with true unmet clinical need, and aim to present our initial findings from the study at a medical meeting later this year," Dr. Goldberg explained.

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HyBryte Trial Halted After Interim Futility Analysis

*By **Dean Patterson***

Soligenix's HyBryte program hit a sharp and unexpected setback after the Data Monitoring Committee recommended stopping the pivotal phase 3 FLASH2 trial due to futility in the treatment of cutaneous T-cell lymphoma (CTCL). The interim efficacy analysis revealed that HyBryte, a topical synthetic hypericin photodynamic therapy (PDT) activated by visible light, did not reproduce the treatment signal seen in the earlier FLASH study despite an 18-week continuous-treatment design intended to support a confirmatory registration path.

"We are obviously very disappointed with the unanticipated outcome of the study," **Christopher J. Schaber, PhD,** president and CEO of Soligenix, said in the company's announcement. He noted that although hypericin PDT previously showed statistically significant lesion reductions after 6 weeks in the first FLASH study, "a similar signal was not observed with 18 weeks of treatment in this study." The company now plans to analyze the dataset, including whether any patient subsets appeared to benefit, before deciding whether to pursue follow-up discussions with the FDA and the European Medicines Agency.

Synthetic hypericin PDT had been positioned as a potentially useful skin-directed option for early-stage CTCL. Current skin-directed therapies can be limited by tolerability, cumulative toxicity, incomplete plaque penetration, or long-term concerns with UV light exposure. The appeal of synthetic hypericin PDT was its mechanism. It is applied topically to lesions and activated about 24 hours later with visible red-yellow light. The company emphasized that this approach avoids UV light–dependent DNA damage and may penetrate more deeply than UV light, which could be relevant for thicker plaques.

The initial placebo-controlled, phase 3 FLASH trial included 166 evaluable patients with stage IA to IIA mycosis fungoides CTCL. After the first 6-week double-blind cycle, 16% of patients treated with hypericin PDT achieved at least a 50% reduction in index lesions as determined by modified Composite Assessment of Index Lesion Severity, compared with 4% receiving placebo. With longer exposure, response rates increased to 40% after two cycles and 49% after three cycles, with responses reported in both patch and plaque lesions. Treatment-related adverse events were mainly mild local skin and application-site reactions, with no drug-related serious adverse events reported.

FLASH2 was meant to confirm that signal. It replicated key elements of the earlier study but extended the double-blind placebo-controlled assessment to 18 weeks of continuous treatment, without the between-cycle treatment breaks included previously. The safety profile remained acceptable in prespecified Data Monitoring Committee evaluations, according to Soligenix, but efficacy did not clear the interim bar.

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Editor's Picks

In each issue of Blood Cancers Today, *we will take a closer look at a particular topic in hematologic malignancies. This month,* Blood Cancers Today *Associate Editor* ***Tycel Phillips, MD,*** *Associate Professor, Division of Lymphoma, Department of Hematology and Hematopoietic Cell Transplantation at City of Hope, highlights recent research in diffuse large B-cell lymphoma (DLBCL).*

Tycel Phillips, MD

Visit bloodcancerstoday.com to stay up to date on the latest news in each area of hematologic oncology.

AGGRESSIVE B-CELL LYMPHOMA

TP53 Allele Burden Sharpens Risk in DLBCL

By ***Dean Patterson***

TP53-mutated DLBCL has long sat in the uncomfortable category of "high risk," but a large integrative analysis suggests the label is too blunt. The biology is worse than average and the outcomes are often poor, but a study published in *Journal of Clinical Oncology*—built from clinical and molecular data on 3,091 patients with newly diagnosed DLBCL across 10 frontline rituximab-based immunochemotherapy cohorts—points to a more nuanced problem: not all *TP53*-mutant disease behaves in the same way, and some of the difference may be measurable at diagnosis.

The researchers examined *TP53* mutations in a setting where they remain common, clinically consequential, and molecularly heterogeneous. *TP53*-mutated disease differed from wild-type disease in the pattern and number of genetic lesions, malignant B-cell expression states, and tumor microenvironment composition. *TP53* mutations were also far more common than *MYC/BCL2/BCL6* double- or triple-hit status, occurring at roughly six times the prevalence, while conferring a similar adverse prognostic risk.

In an interview, study author **Gilles Salles, MD,** a lymphoma specialist and cellular therapist at Memorial Sloan Kettering Cancer Center, indicated that the allele burden may be one of the most practical pieces of information for clinicians.

Gilles Salles, MD

"Overall, *TP53* mutations are associated with poor outcomes, particularly among patients presenting with a high allele frequency," Dr. Salles said, noting that this group represents "nearly half" of patients with detectable *TP53* mutations, which can be identified with standard next-generation sequencing panels or even a dedicated *TP53*-focused assay.

Variant allele frequency (VAF) further separated outcomes among patients with *TP53*-mutant DLBCL. Patients with VAF of at least 75%, a signal consistent with loss of heterozygosity, had significantly inferior progression-free survival and overall survival. In other words, the presence of a *TP53* mutation alone may not be the only indicator of a poor prognosis. The amount of mutant allele and the genomic context around it appear to sharpen the risk estimate.

The study also raises a question many lymphoma clinicians will want answered: should high-VAF *TP53*-mutant DLBCL be treated differently at diagnosis, rather than simply recognized as adverse-risk disease after standard therapy has failed?

One of the more provocative signals came from a re-examination of the PHOENIX trial data. In that analysis, adding ibrutinib to R-CHOP improved progression-free survival in patients with *TP53*-mutant DLBCL and appeared to abrogate the adverse effect of high VAF, regardless of patient age. Dr. Salles called the finding "somewhat unexpected" but said there was "a clear signal" that ibrutinib plus R-CHOP reduced the negative outcome associated with *TP53* mutations in both younger and older patients.

In the PHOENIX trial, patients with non–germinal center B-cell (GCB) disease were enrolled, so the observation cannot simply be generalized across all cases of DLBCL. "The first question is whether this observation can be extended to GCB patients, or other molecular subtypes, and if other BTK [Bruton's tyrosine kinase] inhibitors, covalent or noncovalent, would have the same effects," Dr. Salles said.

The second question may be even more biologically interesting: is the benefit coming from BTK inhibition inside the lymphoma cell, through B-cell–receptor signaling, or from effects on the microenvironment? The molecular data suggest the latter cannot be ignored. *TP53*-mutant samples from patients with poor outcomes, or VAF of at least 75%, showed downregulation of interferon signaling and lower macrophage content. *TP53* mutations were also associated with adverse outcomes within specific LymphGen subtypes, including EZB and MCD; malignant B-cell state S1; and ecotypes LE4, LE7, and LE8. In other molecular contexts, outcomes looked closer to *TP53* wild-type disease.

Dr. Salles said that this "inflammatory and T-cell–depleted" milieu, marked by macrophage activation and interferon-γ signaling, needs to be studied alongside emerging approaches such as bispecific antibodies and antibody-drug conjugates as they move into earlier lines of care.

For now, the practical message is that *TP53* testing may need to become more detailed and specific. Variant allele frequency, molecular subtype, B-cell state, and microenvironmental features may help separate patients who remain candidates for standard frontline approaches from those who should be prioritized for trials of BTK inhibitors, bispecifics, antibody-drug conjugates, or other risk-adapted strategies.

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Patient-Reported Data Favor Fixed-Duration BsAb Therapy in R/R FL and DLBCL

By ***Lauren Evoy Davis***

Researchers conducted a survey of 120 patients with several types of lymphoma to gain insight on how patients feel about the time it takes to receive treatments. This study evaluates patient-reported "time toxicity" associated with bispecific antibody (BsAb) therapies in relapsed or refractory follicular lymphoma (R/R FL) and diffuse large B-cell lymphoma (R/R DLBCL).

Differences in treatment duration and dosing frequency across therapies, including fixed-duration regimens (mosunetuzumab, glofitamab) and continuous treatment (epcoritamab), may significantly influence patient time burden.

Using survey data, the researchers assessed healthcare use, time spent on treatment-related activities, and patient preferences. Results indicated that fixed-duration, less frequently dosed therapies were associated with significantly lower time burden and are strongly preferred by 92% of patients.

Ajay Major, MD, MBA

Ajay Major, MD, MBA, assistant professor, medicine-hematology at the University of Colorado Anschutz spoke with *Blood Cancers Today* (BCT) to give his perspective on these findings.

BCT: **What is the significance of the study's findings?**

Dr. Major: Our study demonstrates that 'time toxicity,' or the time that patients spend receiving cancer care, is a measurable and meaningful patient-centered outcome in patients with lymphoma and differs substantially across different BsAb treatment paradigms. In our patient-reported outcomes study of real-world patients actively receiving BsAb therapies for follicular lymphoma and diffuse large B-cell lymphoma, BsAb treatments, which are administered for a fixed duration and with less frequent dosing, were associated with approximately 50% less time spent on cancer-related care as compared to more frequently-dosed, treat-to-progression BsAb options.

Our study findings provide oncologists and patients with clinically-actionable data to support shared decision-making between different BsAb options and also advances the field of time toxicity research into hematologic malignancies in which ever-growing therapeutic options require a more nuanced understanding of the time burden of our therapies on patients and their care partners.

Do you think it will create more opportunities to ask about patient preferences?

As a lymphoma physician in Colorado, I see patients from all over the time zone, and my patients routinely ask about the expected time burden of different treatments such as BsAb and CAR T-cell therapies—especially when they are traveling many hours from rural areas to the nearest cancer center. Patients and their families actively consider the time they will spend away from work, time spent driving to and from appointments, and the time spent in the infusion chair when they make treatment decisions.

As such, we as oncologists and researchers need data to better counsel our patients about expected time burdens, and our study really allows us to discuss time expectations alongside treatment efficacy and toxicities to more comprehensively address patient preferences about their cancer care.

> **"...'time toxicity,' or the time that patients spend receiving cancer care, is a measurable and meaningful patient-centered outcome in patients with lymphoma..."**

Did anything surprise you about the findings?

The significantly higher hours spent recovering at home with more frequently dosed BsAb options was particularly striking and supports our hypothesis that time toxicity for patients does not just include time in the infusion chair, but also hours of lost work as well as time spent outside of the cancer center working on treatment-related tasks such as appointment scheduling and travel. Further research is needed to fully characterize the relative impacts of these tasks on overall time toxicity, as well as opportunities to better support patients and care partners during treatment.

HemOnc Happenings

Reporting on recent announcements, awards, and appointments in the hematology/oncology sphere

Srinivas Devarakonda, MD, Appointed Chair-Elect of ASCO's IDEA Steering Group

*By **Sara Karlovitch***

Srinivas Devarakonda, MD

Srinivas Devarakonda, MD, an associate professor at The Ohio State University Comprehensive Cancer Center-James Division of Hematology, has been appointed chair-elect of the American Society of Clinical Oncology's (ASCO) International Development and Education Award (IDEA) Steering Group for the 2026-2027 term.[1]

Dr. Devarakonda will serve as chair of the group, which supports the professional development of early-career oncologists from low- and middle-income countries (LMICs) to advance global oncology, in the 2027-2028 term, and will finish his 3-year leadership stint as past chair in the 2028-2029 term. Dr. Devarakonda was first asked to serve as a member of the group in 2023.[2] His expertise is in multiple myeloma, amyloidosis, and bone marrow transplantation.[3]

Founded in 2002, IDEA funds early-career oncologists from LMICs with support from ASCO and Conquer Cancer, the ASCO Foundation.[4,5] The program matches accepted participants with members to expand access to oncology training and mentorship. Those accepted into the program will be able to attend the ASCO Annual Meeting, visit their mentor's institution, and receive 3 years of ASCO membership and a subscription to the *Journal of Clinical Oncology*.[5] The program aims to encourage the exchange of information between participants and their mentors. IDEA and IDEA in Palliative Care fund 30 people to participate in the program annually.

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The Jokes Were Good. The Money Raised Was Better.

*By **Dean Patterson***

Comedy vs Cancer returned to Jazz at Lincoln Center's Frederick P. Rose Hall on April 20 for a sold-out night that raised more than $2.5 million for blood cancer research at Memorial Sloan Kettering Cancer Center (MSK). The benefit, now a familiar meeting point for comedy and oncology philanthropy, has raised more than $9 million for MSK since 2019.

Nick Kroll hosted this year's show, joined by Bridget Everett, Zarna Garg, Brett Goldstein, and Hasan Minhaj. It was the kind of lineup built to fill a room, and it did. But the event's larger purpose was never just the show. Comedy vs Cancer supports early-stage research into blood cancers, including aggressive diseases such as acute myeloid leukemia and multiple myeloma.

Brett Goldstein and Nick Kroll

"Comedy has a unique power to bring people together, even in the face of something as serious as blood cancer," said Kroll, co-founder of Comedy vs Cancer. "Every year, we get to help turn a night of laughter into real hope for patients and their families. At the end of the day, that's what it's all about."

In 2025, money raised by the Comedy vs Cancer community helped launch five new MSK research projects focused on better understanding and targeting of aggressive blood cancers. One project involves engineering an off-the-shelf chimeric antigen receptor T-cell therapy. In another, investigators ask whether lifestyle changes alone may slow cancer progression.

"At a time when funding for research is increasingly uncertain, the generosity of the Comedy vs Cancer community gives our scientists the freedom to ask ambitious questions and pursue discoveries that can genuinely change lives," said **Ivan Maillard, MD, PhD,** head of the Division of Hematologic Malignancies and Laurence Joseph Dineen Chair in Leukemia Research at MSK. "What begins as a bold research question today can become the breakthrough treatment of tomorrow—and that transformation is fueled by philanthropy."

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PHOTO CREDIT: MEMORIAL SLOAN KETTERING CANCER CENTER

figure1

Where Clinicians Come to Collaborate

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figure1