*TRANSLATING HEMATOLOGIC ONCOLOGY DISCOVERIES INTO PRACTICE*

bct
BLOOD CANCERS TODAY

August 2026

bloodcancerstoday.com

When Epstein-Barr Virus Takes a Dangerous Turn
**p. 11**

New Data Clarify Cardiovascular Risks of HMA and Venetoclax in AML
**p. 14**

Impact of Disease Biology in Patients With R/R Myeloma Following CAR-T
**p. 18**

Jorge Cortes, MD, Appointed Chief of Hematology at UAB
**p. 20**

# Gains Made in Management of Novel Therapy Toxicities, but Still More to Be Learned

*With expert opinion from*
**Premal Lulla, MBBS, Shonali Midha, MD, and Gwen Nichols, MD**

MAIL TO:

**HIRA MIAN, MD, MSC:** Advancing Real-World Data in Multiple Myeloma: Closing the Gap Between Trials and the Clinic


PHYSICIAN'S WEEKLY

# HOW AMBIENT AI HELPED SOME CLINICIANS RECONNECT WITH PATIENTS

Medicine was meant to be personal — so when did the screen become the center of care? As physician burnout rises and documentation demands pull clinicians further from patients, one health system's experience suggests technology may be helping medicine rediscover what it lost. Could AI be doing more than saving time? Explore how a new approach to documentation is reshaping the physician-patient connection and restoring meaning to care.

Travis Bias, DO, MPH

www.physiciansweekly.com

# CONTENTS

Volume 5 | Number 8 | August 2026

## Gains Made in Management of Novel Therapy Toxicities, but Still More to Be Learned

Targeted or immunotherapy-based treatments have been added to or have replaced existing standard-of-care regimens across a variety of hematologic malignancies in the last two decades. However, the transition from traditional cytotoxic therapies to novel therapies has brought with it a set of distinct treatment-related toxicities.

7

## Viewpoints

**EDITOR'S MESSAGE**

Advancing Real-World Data in Multiple Myeloma: Closing the Gap Between Trials and the Clinic

2

## GME Spotlight

**FINDING THE OLDER PATIENTS WITH AML WHO GO THE DISTANCE ON IDH INHIBITORS**

Every treatment decision for older patients with *IDH*-mutated acute myeloid leukemia (AML) requires clinicians to navigate a complex road.

4

## Features

**GET TO KNOW**

### Joselle Cook, MBBS

Dr. Joselle Cook shares her community-based research on racial disparities in myeloma.

5

## News

**REGULATORY ACTIONS**

FDA Accepts New Drug Application for Mezigdomide Triplet in Myeloma

10

**MEETING NEWS**

Q&A With Elizabeth Brem, MD: Rethinking the First Move in Large B-Cell Lymphoma

12

**NEWS ROUNDUP**

Prior Authorization Delays Add Complexity to Medication Access and Treatment Decisions

16

**EDITOR'S PICKS**

Cevostamab Draws Durable Responses in Myeloma After BCMA CAR-T Failure

17

**HEMONC HAPPENINGS**

Tycel Phillips, MD, Recognized for Lymphoma Excellence

20

**ONLINE FIRST**

Visit ***bloodcancerstoday.com*** to read everything we couldn't fit in print.

- Q&A: Rethinking the First Move in Large B-Cell Lymphoma
- R-Pola-Glo Improves Quality of Life While Controlling DLBCL in Frail Older Adults

**Sign up to receive our weekly eNewsletters to have the latest headlines delivered to your inbox.**



**PUBLISHER**

Formedics
180 Mount Airy Road, Suite 205
Basking Ridge, NJ 07920

**JOIN BCT ONLINE**

bloodcancerstoday.com
Blood_Cancers
BloodCancersToday
Blood Cancers Today
Blood Cancers Today
Blood Cancers Today

bct
BLOOD CANCERS TODAY
A FORMEDICS PROPERTY

**Subscription inquiries should be sent to:** Subscriptions@Formedics.com
*Blood Cancers Today* is published by Formedics, at
180 Mount Airy Road, Suite 205, Basking Ridge, NJ 07920.
Printed in the USA. 

**Postmaster:** Send address change to: *Blood Cancers Today*, Formedics, 180 Mount Airy Road, Suite 205, Basking Ridge, NJ 07920. 

# Advancing Real-World Data in Multiple Myeloma: Closing the Gap Between Trials and the Clinic

**Hira Mian,** MD, MSc

Clinical trials remain the gold standard for establishing the efficacy of new treatments for multiple myeloma (MM), but many of the patients we treat every day would never have qualified to enroll in them. Anywhere from 50% to more than half of real-world patients with MM are excluded from clinical studies because of age, comorbidities, organ dysfunction, or disease characteristics that make them ineligible. This means that the evidence we rely on to make treatment decisions is often derived from a population that looks quite different from the patients sitting in front of us.

Real-world data have helped address that problem in several ways. Historically, analyses drawn from large EHR databases and disease registries have refined how we dose existing drugs, clarified the toxicity profiles we actually see outside controlled settings, and helped us understand how patients manage—or don't manage—long-term treatment. A good recent example is the question of bortezomib dosing frequency. The retrospective analysis by Hoff and colleagues used Flatiron Health data from nearly 2,500 US patients with newly diagnosed MM and found that once-weekly bortezomib produced comparable real-world progression-free survival and overall survival to twice-weekly bortezomib, with substantially lower rates of peripheral neuropathy (18.5% vs 34.7%; $P<0.001$). This is precisely the kind of confirmation real-world data can provide—not overturning the clinical trial evidence, but validating a practice shift that had already been happening on the ground and giving clinicians the confidence to make it standard.

This kind of evidence generation is particularly important in countries like the United States, where racial and ethnic minorities remain significantly underrepresented in MM clinical trials, even though we know that disease characteristics, treatment response, and toxicity profiles can differ across populations. Non-Latinx Black Americans, for instance, have higher rates of bortezomib-associated peripheral neuropathy. Real-world datasets that reflect the diversity of patients being treated in community and academic practices can reveal these differences in ways that trial populations often cannot. Beyond demographics, the US setting also presents a challenge and an opportunity around treatment sequencing. With the number of active agents now available for MM, there is simply no way clinical trials will ever address every meaningful sequencing question. Real-world data are the only practical means we have for understanding what happens when patients move from one regimen to the next, particularly in later lines where enrollment in prospective studies becomes sparse.

I believe that real-world evidence will become even more critical as use of immunotherapy expands in MM. Novel agents, including bispecific antibodies and chimeric antigen receptor T-cell therapies, have unique and sometimes delayed toxicities that may only become fully apparent once they are used across broader, more heterogeneous patient populations. The toxicity signal captured within the confines of a registration trial is a starting point,

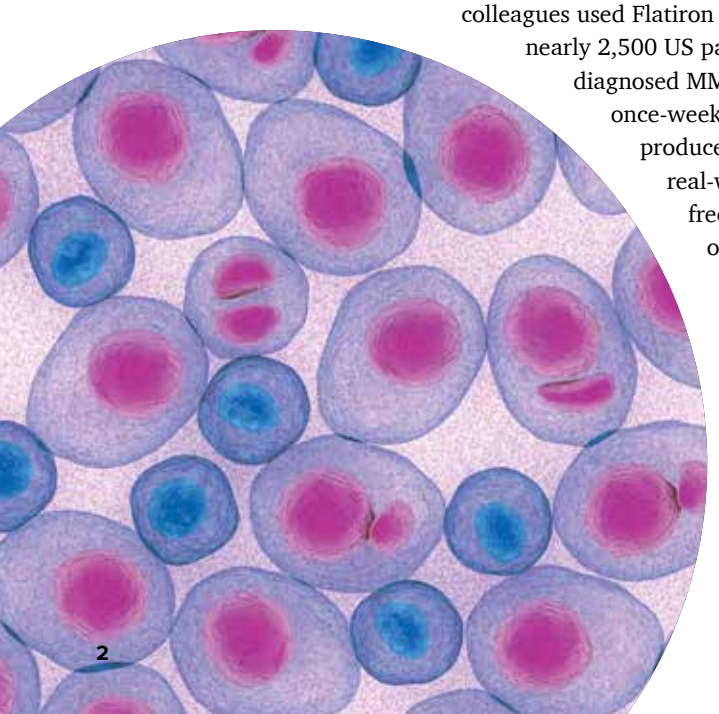


PHOTO CREDIT: ISTOCK.COM/NEMES LASZLO

not a complete picture. Similarly, questions about treatment duration, when to pause therapy because of toxicity, and whether to rechallenge patients who previously had to stop a given agent are areas in which real-world data are already generating hypotheses and will increasingly guide practice.

That said, real-world evidence has real limitations, and clinicians need to read it with those limitations in mind. The patient populations in observational databases are often sicker, more heavily pretreated, or otherwise different from trial cohorts; and these differences are not always predictable or correctable through statistical adjustments alone. Efficacy end points in real-world analyses typically rely on surrogate measures such as time to next treatment rather than progression-free survival based on protocol-specified imaging and laboratory assessments. Toxicity data, too, are almost certainly underreported in most real-world sources; in the Hoff 2024 analysis, the rate of medications initiated for neuropathy was roughly four times higher than the rate of documented neuropathy diagnoses, which tells you something about the incompleteness of administrative coding for capturing clinical events. Disease-specific registries like the Connect® MM Registry, the Indiana Myeloma Registry, and the Center for International Blood & Marrow Transplant Research registry tend to have richer clinical detail than administrative claims sources, but they each have their own selection biases and may not be generalized across settings.

The answer is not to rank real-world data above or below clinical trial evidence, but to use them together and to be clear about what each can and cannot tell us. When a real-world analysis confirms something we suspected, as with once-weekly bortezomib dosing, it strengthens practice. When it raises a new question about a population or a drug use pattern that trials never addressed, it points to where prospective work is needed. As the therapeutic options in MM continue to grow, so does our responsibility to understand how those options actually perform for the full range of patients we treat. That is what real-world data are for.

PHOTO CREDIT: iSTOCK.COM/FROM TOP TO BOTTOM: CHET FROHLICH PHOTOGRAPHY, INC.; ART WAGER; FANI KURTI; HALBERGMAN; ELOI_OMELLA

# Calendar

**September 9–12**
**Society of Hematologic Oncology (SOHO) Fourteenth Annual Meeting**
Houston, TX

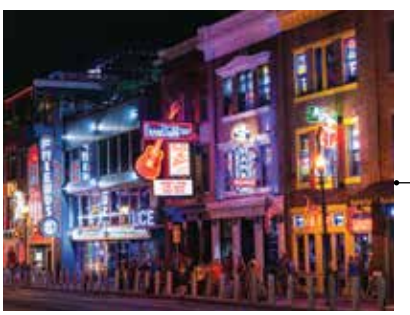
**September 11–13**
**Association of VA Hematology/ Oncology (AVAHO) 21st Annual Meeting**
Austin, TX

**September 18–19**
**8th Annual The Leadership, Empowerment, And Development (LEAD) Conference**
Washington, DC

**September 18–19**
**NCCN 2026 Annual Congress: Hematologic Malignancies**
New York, NY

**October 13–16**
**Lymphoma, Leukemia & Myeloma Congress**
New York, NY

**October 15–17**
**The 9th Annual Meeting of the International Academy for Clinical Hematology (IACH)**
Paris, France



**October 16–17**
**2026 National Summit on Hematologic Cancers**
Nashville, TN

**October 22–23**
**5th European Congress on Hematology and Blood Disorders**
Barcelona, Spain

**October 23–27**
**European Society for Medical Oncology (ESMO) Annual Congress**
Madrid, Spain

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

# Finding the Older Patients With AML Who Go the Distance on IDH Inhibitors

*By* ***Nichole Tucker***

Every treatment decision for older patients with *IDH*-mutated acute myeloid leukemia (AML) requires clinicians to navigate a complex road. For years, the challenge has been balancing disease control with the toxicities associated with venetoclax plus azacitidine, including substantial risks for myelosuppression and infection. Although IDH inhibitors have created a new treatment avenue for this population, the long-term outcomes for patients receiving these targeted therapies have remained a clinical blind spot.

A new single-center retrospective analysis helps bring this previously unseen stretch of road into focus, suggesting that a subset of older adults with *IDH*-mutated AML may achieve exceptionally durable remissions with prolonged IDH inhibitor therapy. In this highly selected cohort, patients continued treatment for a median of nearly 7 years, with survival outcomes that compared favorably with previously reported data, including findings from the AGILE trial (NCT03173248).

Nilesh Kapoor, MD

"In clinical practice, we were seeing that some older patients were on these IDH inhibitors for years," said lead investigator **Nilesh Kapoor, MD,** chief resident of Quality and Patient Safety in the Department of Internal Medicine at UT Southwestern Medical Center, in an interview with *Blood Cancers Today*. "In older patients, we always worry about balancing toxicity with quality of life. We wanted to describe these patients who were tolerating these therapies for quite a while and see whether we could identify long-term responders."

Dr. Kapoor and colleagues conducted a retrospective study of patients aged 65 years and older with newly diagnosed or relapsed or refractory *IDH*-mutated AML who continued uninterrupted ivosidenib or enasidenib therapy for at least 2 years after achieving complete remission (CR) or while receiving maintenance therapy in CR.

Because enrollment required prolonged treatment exposure and remission, the cohort represents a group of exceptional responders rather than the broader population of older adults with *IDH*-mutated AML, the study investigators stress. However, the findings provide important insight into the potential durability of targeted therapy for selected patients and raise questions about how clinicians may better identify individuals most likely to benefit from this treatment approach.

The study included nine patients. The median duration of IDH inhibitor therapy was 6.88 years (range, 1.94-8.87 years), and the median age at treatment initiation was 71 years (range, 65-84 years). Four patients were aged 75 years or older. Six patients had *IDH1*-mutated AML and three had *IDH2*-mutated disease. Four patients initiated treatment with an IDH inhibitor at diagnosis, three after relapse, and two as maintenance therapy after their first CR.

At a median follow-up of 6.88 years (range, 2.62-8.87 years), seven patients (78%) continued IDH inhibitor therapy and still had a CR. The two patients who experienced relapse both had antecedent myeloid neoplasms. Median event-free survival and overall survival were not reached. Estimated 5-year event-free survival was 78% (95% CI, 55%-100%), and estimated 5-year overall survival was 88% (95% CI, 67%-100%).

The investigators also observed no co-occurring receptor tyrosine kinase pathway mutations among the cohort and no cases of differentiation syndrome during prolonged treatment.

For Dr. Kapoor, the next step is identifying which patients are most likely to experience these durable responses.

"What we hope this study accomplishes is identifying patients in the future who may be able to remain on these therapies for quite a while and potentially spare them from more intensive approaches in a way that also preserves their quality and quantity of life," he said.

Future research should focus on identifying long-term responders earlier in the disease course so clinicians can better individualize therapy, according to Dr. Kapoor. By better understanding which patients are most likely to achieve durable benefit, clinicians may be able to make more informed treatment decisions and provide a clearer path forward for older adults with *IDH*-mutated AML. Although prospective studies are needed, these findings offer an important first step toward refining how clinicians navigate treatment choices for this population.

**REFERENCE:**

Kapoor N, et al. *Leuk Res.* 2026;167:108268. doi:10.1016/j.leukres.2026.108268

# Get to Know

*Learn more about the leaders, innovators, and educators in hematologic oncology*

PHOTO CREDIT: @JOSELLECOOKMD ON X

## Joselle Cook, MBBS

Joselle Cook, MBBS, an assistant professor of medicine at Mayo Clinic in Rochester, Minnesota, describes her community-based research on racial disparities in multiple myeloma, her family history with cancer, and how she integrates her fitness hobbies into her career to inspire patients.

### From Caregiver to Clinician

Before becoming a hematologist oncologist, **Joselle Cook, MBBS,** had already known the weight of caring for someone with cancer.

Her father was diagnosed with colon cancer when she was a late teen, which spurred her interest in oncology. By the time she started medical school at the University of the West Indies, she became his full-time caregiver until he passed away during her time at medical school.

"That gave me a deep perspective on being a caregiver and having a relative with cancer," she reflected. "That's a big reason why I'm in this field today. I have not only the clinician perspective, but also the caregiver burden perspective and all the considerations of taking care of a patient with progressing cancer. I value that experience."

Originally from Trinidad and Tobago, Dr. Cook later pursued her residency at Kings County Hospital in New York, where she saw patients with advanced-stage multiple myeloma.

"That developed further during my fellowship at Mayo Clinic, where I had so many questions about multiple myeloma," Dr. Cook explained. "Why did some populations develop this more than others? The life expectancy was rapidly changing due to changes and advancements in therapies, which also piqued my interest."

"I had great mentors that supported me along this journey," she continued, crediting Dr. Martha Lacy as her first mentor in oncolytic viral therapy and Drs. Vincent Rajkumar and Shaji Kumar as pivotal mentors in plasma cell disorders. "It was a combination of opportunity, mentorship, and exposure."

### Racial Disparities in Myeloma: Community-Based Research

Towards the end of her fellowship, Dr. Cook sought to answer the question: "Why are Black individuals disproportionately impacted by hematologic malignancies?"

"We have a large East African population here in Minnesota that's never been studied," Dr. Cook explained. "With my mentors, Dr. Shaji Kumar and Dr. Vincent Rajkumar, we asked: 'What is the prevalence of myeloma in this cohort? Is the risk the same for all African ancestry individuals?'"

To answer these questions, Dr. Cook and her mentors embarked on the MAGIC study (MGUS [Monoclonal Gammopathy of Undetermined Significance]/Myeloma Awareness and Genetic Insights Campaign), a community-driven, education-focused screening study to determine the

prevalence of monoclonal gammopathies such as MGUS, myeloma, and smoldering myeloma across diverse populations in Minnesota. Results will be presented later in 2026.

"We're finding that the prevalence is quite different from what we expected," she explained. "We figured because of the genetics, [the population] would be somewhere in between African American, which is West African enriched, and White individuals, but they're actually much closer to White individuals or European ancestry in terms of prevalence, which is really interesting. We have the genetics and the genotyping to further understand this, and there will be more data to come."

Dr. Cook described the process of collecting data for a community-driven study as a learning journey that involves developing and retaining community trust while understanding why certain populations are hesitant to participate in research.

**"There are disparities in the prevalence of multiple myeloma, but there are also disparities in health literacy and access to care. If we improve health literacy ... then maybe we could improve outcomes and prevent later presentations of myeloma when it does occur."**

"I learned that you can't just go into the community and expect to get samples," she said. "The amount of work that goes into community outreach is understated. I did not realize it was going to be this much work, but I learned a lot, and it's helpful for the communities. There are disparities in the prevalence of multiple myeloma, but there are also disparities in health literacy and access to care. If we improve health literacy, which is what I'm trying to do with my education-based screening program, then maybe we could improve outcomes and prevent later presentations of myeloma when it does occur."

### T-Cell Therapies for Myeloma: Improving Access to Bispecific Antibodies

In her new role as director of cell therapy education at Mayo Clinic, Dr. Cook aims to revamp training protocols for different cell therapies such as bispecific antibodies and chimeric antigen receptor (CAR) T-cell therapy.

"In the field of myeloma, we're trying to understand where bispecific antibodies fall into the treatment paradigm," she said. "There is a big question in the field: should you do bispecifics or CAR-T first? Right now, CAR-T is preferred first, but we are still trying to understand which one to do first. CAR-T has been incredible in giving deep responses and long responses, but there are patients who don't want CAR-T and patients for whom CAR-T is not feasible. Bispecific antibodies can improve access to novel therapies for patients."

Dr. Cook is working with the American Society of Hematology (ASH) to improve access to bispecific antibodies for patients outside academic centers by pioneering and implementing a 24-hour remote patient monitoring program to safely monitor for adverse events.

"One of the biggest issues with bispecific therapy is the risk of cytokine release syndrome, which can cause side effects such as fever and low blood pressure. As a result, bispecifics are given in incremental step-up doses," she explained. "Because of that risk of cytokine release syndrome, many community sites are reluctant to give it. These are usually given at academic centers with hospitalization. However, hospitalization reduces access to care because patients have to be close to an academic center and take time off work to be at that academic site for about 2 weeks for this type of dosing period. Many academic sites are fully equipped to do this, but community sites are not."

According to Dr. Cook, safely implementing bispecific antibodies outside academic centers requires helping community sites build treatment plans, prophylactic measures and contingency plans for cytokine release syndrome, and remote monitoring capabilities with a virtual, off-site platform in the absence of medical staff. She is also working closely with partner sites in California and North Carolina.

"Once this is done through ASH and completed, then it would be proof of concept that this can be done safely and that novel therapies can be accessible to people regardless of their location," Dr. Cook said.

### From Weight Bench to Bedside

Balancing work and family life as a soccer mom to her 15-year-old daughter, Dr. Cook describes herself as a micro fitness influencer under the Instagram handle @the_fit_oncologist. Whether it's showing her gym progress or sharing the anti-cancer benefits of creatine, Dr. Cook posts fitness-related content to help motivate others. From weight bench to bedside, she brings this same passion to the clinic to inspire patients and teach them about the importance of health and diet.

"I enjoy talking to my patients about fitness, diet, and lifestyle," she said. "I use 'The Fit Oncologist' as a platform to show what life is. You can have some balance as a hematologic oncologist, but you can also work out and be healthy. It helps me be a good example to my patients. As patients with myeloma continue to live longer after CAR-T therapy and they start to feel normal and healthy again, they always ask, 'What can I do differently?' It's a good opportunity for me to talk about exercise and diet. I really enjoy that aspect of treating patients with myeloma."

**REFERENCE:**

ClinicalTrials.Gov. Accessed August 10, 2026. https://clinicaltrials.gov/study/NCT06472830

# Gains Made in Management of Novel Therapy Toxicities, But Still More to Be Learned

*By* ***Leah Lawrence***

Targeted or immunotherapy-based treatments have been added to or have replaced existing standard-of-care regimens across a variety of hematologic malignancies in the last 2 decades. As a result, survival has improved substantially, although to varying degrees, across many of these malignancies, including multiple myeloma, non-Hodgkin lymphoma, and acute leukemias.[1] However, the transition from traditional cytotoxic therapies to novel therapies has brought with it a set of distinct treatment-related toxicities.

*Blood Cancers Today* recently spoke with several experts about the toxicities associated with these novel agents, how these toxicities are recognized and managed, and the role they play in treatment selection.

## Acute Toxicities

Chimeric antigen receptor (CAR) T-cell therapy has been one of the most impactful novel treatment strategies for hematologic malignancies in recent decades. First approved for B-cell acute lymphoblastic leukemia (ALL) by the FDA in 2017,[2] there are now seven approved CAR T-cell therapies spanning multiple myeloma, ALL, mantle cell lymphoma, follicular lymphoma, large B-cell lymphoma, and marginal zone lymphoma.[3]

"The two common acute toxicities associated with CAR T-cell therapy are cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), and they were as new to most hematologist/

ILLUSTRATION BY JOHN SALESI

oncologists as the therapy was," said **Premal Lulla, MBBS, MS,** associate professor in the Center for Cell and Gene Therapy at Baylor College of Medicine. "These toxicities were not fully predicted from preclinical studies and were surprising, but now with over a decade of use, Centers are more familiar with how to handle them."

CRS of any grade occurs in approximately 50%-60% of patients who undergo CAR T-cell therapy.[4] The incidence and severity of CRS vary across specific therapies and occur mostly within the first week or two after infusion.[5]

"Coinciding with the approval of CAR T-cell therapy was the cytokine blocking agent tocilizumab for the management of CRS, with initial studies showing a remarkable efficacy for reducing fevers," Dr. Lulla said. "There was some consternation about using cytokine blocking agents because of fear that the intervention would diminish the CAR T-cell therapy, but those fears seem to have quelled."

The incidence of ICANS is less, with ICANS of any grade estimated to occur in about one-quarter of patients who undergo CAR T-cell therapy.[6] Tocilizumab can also be used when ICANS occurs in conjunction with CRS, but most cases can be effectively managed with supportive care and steroids.[7]

Clinicians also gained experience with the management of CRS and ICANS among patients undergoing treatment with bispecific antibodies. Within multiple myeloma, for example, there are currently four FDA-approved bispecific antibodies: three targeting B-cell maturation antigen (BCMA) and CD3 (teclistamab, elranatamab, and linvoseltamab) and one targeting GPRC5D and CD3 (talquetamab).[8]

"In regard to class-wide toxicities, similar to any T-cell engaging therapy, we do see CRS and, to a lesser extent, ICANS, although in many cases to a lesser grade," said **Shonali Midha, MD,** a medical oncologist at Dana-Farber Cancer Institute. "Many studies have shown that the use of prophylactic tocilizumab or other prophylactic measures have been effective in mitigating that side effect."

Recent research has even explored the use of a single prophylactic low dose of tocilizumab and found it effectively reduced CRS during step-up dosing, demonstrating how clinicians continue to improve management strategies for these side effects.[9]

Patients taking bispecific antibodies may also experience on-target but off-tumor toxicities. For example, therapies targeting GPRC5D can trigger adverse events affecting the skin, nails, and taste perception, Dr. Midha explained.

"We commonly see skin, nail, or hair changes, many of which we can try to prevent with the use of moisturizing creams, vitamin-E based nail hardeners, and use of good oral hygiene and non-alcohol based mouth rinses," Dr. Midha said. "In cases of dysgeusia, which can lead to significant weight loss, you will want to discuss mitigation strategies, and that may involve a meeting with a nutritionist."

Some other novel therapies for hematologic malignancies result in some off-target toxicities, such as ocular adverse effects. For example, the antibody drug conjugate belantamab mafodotin, approved for multiple myeloma, is associated with risk for corneal epithelial toxicity, which can be severe and dose-limiting.[10]

"We work closely with nursing, pharmacy, and nutrition teams when it comes to these and other toxicities that are drug or drug-class specific," Dr. Midha said. "At our institution, we have come up with guidelines for how to prevent these toxicities, when possible, and for their treatment based on information from clinical trials that have included these medications or others with similar toxicities."

### More Use, More Knowledge

"To my knowledge, the therapies that are being developed in these areas are now less toxic than before as research finds ways to eliminate some of the known toxicities," said **Gwen Nichols, MD,** chief medical officer at Blood Cancer United.

One example of this is the evolution of Bruton's tyrosine kinase (BTK) inhibitors, a class of drugs used in the treatment of chronic lymphocytic leukemia and mantle cell lymphoma. The first-generation BTK inhibitor ibrutinib was found to have off-target effects on the cardiovascular system, carrying risk for atrial fibrillation, heart failure, and hypertension.[11] However, second-generation BTK inhibitors, such as acalabrutinib or zanubrutinib, are associated with fewer cardiovascular toxicities with less treatment-limiting toxicity.[12]

Additionally, growing use and the passage of time have allowed some research into the late effects of these novel therapies. A meta-analysis published in 2024 found that CAR T-cell specific toxicities like CRS and ICANS accounted for a minority of nonrelapse mortality; instead, more than half of the reported nonrelapse deaths were a result of infection.[13]

"CAR T-cell therapy destroys or eliminates B-cells that make protective antibodies," Dr. Lulla said. "We didn't fully understand the risk for infection, but now know that hypergammaglobulinemia and duration of cytopenia can be unexpectedly long after CAR T-cell therapy."

Infection is also a risk for patients treated with bispecific antibodies, according to Dr. Midha.

"We do know that decreasing the frequency of dosing can sometimes mitigate the risk of infection, as can the use of prophylactic medications or intravenous immunoglobulin [IVIG] therapy," Dr. Midha said.

Delayed neurotoxicity is sometimes seen 3 to 6 months after treatment with BCMA-targeting CAR T-cell therapy for myeloma, according to Dr. Lulla.

"It is rare, occurring in less than 5% of patients, and we now know that if you give patients adequate bridging therapy to control the disease, you can essentially avoid this toxicity," Dr. Lulla said.

Another emerging "clinically relevant" late toxicity associated with CAR T-cell therapy and bispecific antibodies is risk for secondary malignancy.[14,15] In 2024, the FDA posted a safety communication about reports of T-cell malignancies in patients who had received BCMA- or CD19-directed CAR T-cell therapy, but Dr. Lulla emphasized it is an "extremely rare complication."[14]

"We published our own center's outcomes of more than 300 CAR-T recipients and saw zero cases of CAR-expressing secondary malignancy cells, i.e. where the secondary cancer cells express the CAR molecule" Dr. Lulla said. In the cases where it has been identified, it has not been proven whether it was linked directly to the engineering of the cells to express the CAR molecule or that the CAR expression by these cancer cells is a bystander effect. "In the grand scheme of things I tell patients, 'We have to treat the cancer in front of you, not prevent the future cancer that may or may not develop.'"

### More Information Needed

Patients and physicians will need to have shared decision-making conversations to discuss the potential for these and other toxicities related to novel treatment approaches to hematologic malignancies.

"Patients have different goals or criteria in mind when looking at several different therapy options," Dr. Midha said. "These play a role in decision-making, as well as a patient's prior therapies, exposure to certain classes of drugs, and the pace of disease relapse."

Dr. Nichols also emphasized the need to discuss potential side effects with family and caregivers.

"For example, if the patient has a mental status change, they may not know they are febrile," Dr. Nichols said.

Finally, it will be important to gain more knowledge about the potential for late toxicities, especially when having decision-making conversations with adolescent and young adults patients with hematologic malignancies.

"We know the long-term toxicities of chemotherapy on the heart, the kidneys, on the nerves, but we haven't been using these immunotherapies—particularly CAR T-cell therapy—long enough to know whether there are going to be autoimmune side effects for kids, or changes in their ability to fight infections in the future," Dr. Nichols said.

Blood Cancer United is working on several ways to find out more about the prevalence and potential for some of these late toxicities.

"One great concern is fertility and how these treatments impact the ability to conceive and bear children, and any effect on those children," Dr. Nichols said. "We have a fertility registry for people who have undergone CAR T-cell therapy where patients can join and report information."

Blood Cancer United is also supporting a research consortium among pediatric hospitals that are researching immune status and long-term follow-up in children who have undergone CAR T-cell therapy.

"For a patient undergoing these treatments when they are 60, what happens in 25 years may be much less critical, but for a child who undergoes treatment at 5 years old, what happens 25 years later affects them when they are only 30," Dr. Nichols said. "We need to better understand how these therapies impact people, especially children, long-term."

**REFERENCES:**


1. Woodson K, et al. *Cureus*. 2026 Jun 30;18(6):e111845. doi: 10.7759/cureus.111845
2. FDA. Accessed July 28, 2026. https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/August-30--2017-Summary-Basis-for-Regulatory-Action---KYMRIAH.pdf
3. FDA. Accessed July 28, 2026. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products
4. 65th American Society of Hematology Annual Meeting. Abstract 5150. https://www.postersessiononline.eu/173580348_eu/congresos/ASH2023/aula/-MON_5150_ASH2023.pdf
5. Ahmed N, et al. *Blood Adv.* 2024 Oct 22;8(20):5346-5354. doi: 10.1182/bloodadvances.2023012549
6. Han MW, et al. *Front Neurol.* 2024 Oct 15:15:1392831. doi: 10.3389/fneur.2024.1392831
7. Jain MD, et al. *Blood.* 2023 May 18;141(20):2430-2442. doi: 10.1182/blood.2022017414
8. ASCO Daily News. Accessed July 28, 2026. https://dailynews.ascopubs.org/do/earlier-use-bispecific-antibodies-multiple-myeloma-current-data-and-remaining-questions
9. Hamadeh IS, et al. *Clin Lymphoma Myeloma Leuk.* 2026 Jun;26(6):e802-e810. doi: 10.1016/j.clml.2026.03.016
10. Aqil MS, et al. *Front Oncol.* 2026 Jan 6;15:1691518. doi: 10.3389/fonc.2025.1691518
11. Quartermaine C, et al. *JACC CardioOncol.* 2023 Oct 17;5(5):570-590. doi: 10.1016/j.jaccao.2023.09.002
12. Mushtaq A, et al. *Oncologist.* 2026 Mar 23;31(5):oyag102. doi: 10.1093/oncolo/oyag102
13. Cordas Dos Santos DM, et al. *Nat Med.* 2024 Sep;30(9):2667-2678. doi: 10.1038/s41591-024-03084-6
14. FDA. Accessed July 28, 2026. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-requires-boxed-warning-t-cell-malignancies-following-treatment-bcma-directed-or-cd19-directed
15. Tomasik J, et al. *JAMA Oncol.* 2026 Jun 18:e261859. doi: 10.1001/jamaoncol.2026.1859

# Regulatory Actions

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

Scan to learn more.

*June 17, 2026*

## FDA Accepts Supplemental BLA for Mosunetuzumab Plus Polatuzumab Vedotin for Relapsed or Refractory Large B-Cell Lymphoma

Based on data from the phase 3 SUNMO study, the FDA has accepted a supplemental Biologics License Application (BLA) for mosunetuzumab in combination with polatuzumab vedotin for patients with large B-cell lymphoma who received at least one prior line of therapy. The FDA target action date is February 9, 2027.

*June 26, 2026*

## FDA Approves Pen Device for Adult Patients With Polycythemia Vera

The FDA has approved a ropeginterferon alfa-2b-njft pen device (BESREMi Pen) for adult patients with polycythemia vera, a prefilled device that allows for patient self-administration. Biopharmaceutical company PharmaEssentia has also submitted a BLA to expand the label to include patients with essential thrombocythemia.

*June 19, 2026*

## Tafasitamab Plus Lenalidomide Approved in Japan for Adult Patients With Relapsed or Refractory DLBCL

Japan's Ministry of Health, Labour and Welfare has approved tafasitamab plus lenalidomide for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) based on results from the international L-MIND study and the national J-MIND study in Japan.

*July 6, 2026*

## European Commission Approves Epcoritamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma

The approval is based on the phase 3 EPCORE FL-1 trial, which showed that epcoritamab plus lenalidomide and rituximab reduced the risk of disease progression or death by 79% compared with lenalidomide and rituximab alone. The combination was approved in the United States in November 2025.

*July 13, 2026*

## FDA Accepts New Drug Application for Mezigdomide Plus Carfilzomib and Dexamethasone for Relapsed or Refractory Multiple Myeloma

The FDA's decision is based on results of the phase 3 SUCCESSOR-2 trial, in which mezigdomide plus carfilzomib and dexamethasone showed a statistically significant progression-free survival improvement compared with carfilzomib and dexamethasone alone. The target action date is May 13, 2027.

Highlights from the **2026 PAN PACIFIC LYMPHOMA CONFERENCE,** July 20–24, 2026, in Kohala Coast, Hawaii

# When Epstein-Barr Virus Takes a Dangerous Turn

*By **Nichole Tucker***

Epstein-Barr virus (EBV) in most individuals remains contained, a controlled ember that never becomes a fire. In rare cases, the containment fails, allowing immune activation to escalate into a life-threatening disease process—chronic active EBV, which demands rapid recognition and expedited treatment to improve patients' chances of cure.

"Getting the patient to a transplant center is the central focus of management," said **Jennifer A. Kanakry, MD,** medical director of the Stem Cell Transplant and Cellular Immunotherapy Program at MedStar Georgetown University Hospital, in an interview with *Blood Cancers Today.* At the 2026 Pan Pacific Lymphoma Conference, she focused on helping clinicians recognize chronic active EBV earlier and move patients toward appropriate care.[1]

Jennifer A. Kanakry, MD

### Tracing the Origin

Dr. Kanakry emphasized that chronic active EBV (CAEBV) is not a single disease, but rather a group of related disorders with distinct clinical features and treatment considerations. Understanding whether EBV is affecting B cells or T/NK cells is critical, as the two forms follow different disease pathways and require different approaches to care. B-cell CAEBV, which is more commonly recognized in the United States, typically affects young adults and may present with symptoms such as splenomegaly and lymphadenopathy. In contrast, T/NK-cell CAEBV is a WHO-defined, highly aggressive disorder that is more common in children and can lead to severe immune dysregulation, hemophagocytic lymphohistiocytosis, organ failure, and progression to NK/T-cell lymphoma. "Because chronic active EBV disease can present differently, the management of the disease cannot be universal," Dr. Kanakry explained.

For patients with T/NK-cell CAEBV, the challenge lies in a fundamental breakdown of immune control. The immune system can no longer effectively recognize and eliminate EBV-infected T or NK cells, allowing these abnormal populations to persist, expand, and drive ongoing disease. As Dr. Kanakry explained, "The best way to kill a T cell is with another T cell."

This breakdown in immune surveillance helps explain why allogeneic hematopoietic cell transplantation (HCT) remains the cornerstone of treatment. By introducing a healthy donor immune system, HCT can provide the immune cells needed to recognize and eliminate abnormal EBV-infected cells.

Antiviral therapies have limited benefit once T/NK-cell CAEBV is established because they do not correct the underlying immune dysfunction driving the disease. "Allogeneic hematopoietic cell transplantation can replace a dysregulated immune system with a healthy immune system, providing the only potential cure for T-CAEBV," Dr. Kanakry emphasized.

### Extinguishing the Flames

Recent clinical guidelines suggest how clinicians should approach CAEBV management.[2] Dr. Kanakry calls it "the 3-step approach." First, clinicians must cool down the temperature coming from the flames. This entails treating hemophagocytic lymphohistiocytosis, immune dysregulations, and organ dysfunction. This involves careful administration of steroids, cyclosporine and etoposide, treatment with pegaspargase, tracking CXCL9 levels, and administering emapalumab to suppress the IFN-gamma pathway.

Cytoreduction, step 2, serves as an important containment step, reducing the population of abnormal EBV-infected cells before the immune system can be rebuilt through allogeneic HCT. The guideline-recommended method is administration of CHOP or another chemotherapy regimen followed by central nervous system evaluation and intrathecal chemotherapy.

The final step is reconstruction through allogeneic HCT, rebuilding the immune system with donor-derived cells that can restore control over EBV and provide the only potential path to cure. According to the data, the 3-step approach has a 3-year overall survival rate of 87% compared with 17% for those who are transplanted without the 3-step approach, Dr. Kanakry explained.[3]

Because T/NK-cell CAEBV can progress rapidly, Dr. Kanakry emphasized that referral should occur early, allowing time for disease control, donor selection, and transplant planning before the window for curative therapy starts to close.

**REFERENCES:**

1. Kanakry J. 2026 Pan Pacific Lymphoma Conference.
2. Kawada Ji, et al. *Int J Hematol.* 2023;118(5):568–576. doi:10.1007/s12185-023-03660-5
3. Sawada A, et al. *Int J Hematol.* 2017;105(4):406-418. doi:10.1007/s12185-017-2192-6

## Rethinking the First Move in Large B-Cell Lymphoma

*By **Nichole Tucker***

Many patients with large B-cell lymphoma still receive standard chemoimmunotherapy, but physicians are increasingly weighing unique patient needs and the potential impact of first-line choices on future therapeutic options. At the 2026 Pan Pacific Lymphoma Conference, **Elizabeth Brem, MD**, discussed how these considerations are influencing the management of newly diagnosed large B-cell lymphoma and where the field may be headed.

Elizabeth Brem, MD

In this interview, Dr. Brem shares how she approaches frontline treatment selection, incorporates biologic and patient-specific risk factors into her clinical decision-making, and anticipates treatment sequencing as novel therapies move into earlier lines of care.

***Blood Cancers Today:*** **When you're sitting across from a newly diagnosed patient with large B-cell lymphoma, what is the very first question you try to answer before you even think about selecting a regimen?**

**Dr. Brem:** We talk about this a lot with our older patients, but I think we do this internally with patients of any age, which is assess what their other medical problems are and what we call *functional status* or how much they can do right now. And with that, you try to assess how much of that is from the lymphoma. Because we have many people who come to us with large B-cell lymphoma who felt fine 3 months ago. Everything has fallen apart over those last few months, and you feel quite certain it's from the lymphoma.

In which case you feel like, yes, I might have to give them some toxicities from the chemotherapy, but if I can get them through that, I can get them back to a very stable baseline, once I get rid of the thing that's making them feel so poorly, versus somebody who maybe already was wheelchair bound at baseline. Although they may not feel great from their lymphoma, a lot of their current limitations are due to other medical problems rather than the lymphoma, and that will affect how you might want to treat that patient.

**The conversation around frontline therapy has shifted over the past few years. What factors today have the greatest influence on whether a patient receives a newer regimen versus a more traditional approach?**

You'll get different answers to this question if you ask different lymphoma doctors. But for me, a lot of it comes from the POLARIX study. We now have 6 years of follow-up from that trial, and it was R-CHOP versus Pola-R-CHP. There was an advantage in progression-free survival with the POLA-based regimen. Initially, there were worries about toxicities. There was discussion about cell of origin. Is POLA better for some patients than others? I think finally where I have landed, after sitting with this for a while, is anybody who could have gone on that trial, which is anybody with newly diagnosed diffuse large B-cell lymphoma in relatively decent shape who had an IPI [International Prognostic Index] of 2 or greater, probably should get Pola-R-CHP.

Does it seem like it maybe benefits certain patients, this non–germinal-centered subtype a little bit more? Yes. However, we don't know that it doesn't benefit the other patients. The toxicity profile is similar, and the way most of us assess cell of origin in our clinic is different than the way it was done in the trial. So, it's really hard to know if that tool that they use there, this kind of whole-genome sequencing, [is going] to identify cell of origin. Our tools might be misclassifying patients. So, for me at this point in time, if somebody really could have gone on that trial, I really do favor the polatuzumab-based regimen for those patients.

There are still patients who do benefit from good old-fashioned R-CHOP: certainly patients with lower International Prognostic Index (IPI) scores, anybody who you're worried would have risk of gastrointestinal toxicity from the polatuzumab (I have definitely seen diarrhea and manage more nausea with that regimen), and anybody who you're going to do an abbreviated course of chemotherapy for. There are a couple of studies that suggest that for very select patients with very limited-stage disease, you can get away with four rounds. All of those trials were done with R-CHOP. You could extrapolate—maybe it would be similar with POLA—but I certainly still do R-CHOP for those patients who I'm assuming may get limited duration of therapy. I practice in a hospital where I have limited access to polatuzumab, so [if] for whatever reason I'm treating someone in house, I will still use R-CHOP, and then sometimes I'll switch it to the POLA after discharge.

For older patients, the standard at this moment is still what's called R-mini-CHOP, which is not quite but almost a 50% dose. There is an ongoing study looking at the R-mini-CHOP versus R-mini-POLA CHP, so the mini version of that regimen. We have not seen that data yet. I do know people who do use the R-mini-POLA CHP–type regimen. I personally don't at this moment until I see the data from the POLAR-BEAR study, which I'll always be jealous of because I think it's one of the best trial names. For me, I still use R-mini-CHOP in my older patients, but I have seen variability in how other people manage that.

**Risk stratification continues to evolve. Beyond the International Prognostic Index, are there biologic or clinical features that have become particularly influential in your decision-making?**

The biggest one we all still worry about is what's called double-hit lymphoma. Classically, that's a translocation in *BCL-2 MYC*. Sometimes it's *BCL-6* and *MYC*—not 100% clear if that's quite as bad of an actor—but many people worry about it. For those patients, most of us still use dose-adjusted EPOCH [etoposide, prednisone, Oncovin (vincristine), cyclophosphamide, and Hydroxydaunorubicin (doxorubicin)], which is certainly for the broader population in a large, randomized trial; [it is] more toxic and does not necessarily lead to better outcomes compared to R-CHOP. But for these double-hit, triple-hit patients, most of us still do use dose-adjusted EPOCH.

Otherwise, it's really interesting. We started with this; everybody got CHOP, and then we started to slice it off with different IPI or different cells of origin. I wonder if we're actually going to start narrowing things again. There are a couple trials that haven't read out yet. There's one called ESCALADE that's going to add acalabrutinib to R-CHOP, but only in the ABC, or activated B-cell, subtype patients. We'll see what happens with that trial. There's another trial that just read out called frontMIND using tafasitamab. Everybody thought maybe that was going to be more beneficial in the germinal center patients in that large, randomized trial. It wasn't.

We're going to see readout in the next wave of trials, including next-generation CELMoDs [cereblon E3 ligase modulatory drugs] plus R-CHOP, bispecific antibodies being utilized in the frontline setting. I'm wondering if those are going to make the cell-of-origin piece a little bit irrelevant, because many of these approaches you would expect to work regardless of what cell of origin the lymphoma is. So, I feel like we went from R-CHOP to it getting really complicated. Who gets CHP, Pola-R-CHP? Who gets R-CHOP? Who gets dose-adjusted EPOCH? I think we're going to start swinging back towards a simpler thing where maybe cell of origin doesn't matter as much, and most advanced-stage patients are going to end up getting relatively similar therapy.

**Lymphoma specialists often discuss the "best" regimen, but there are different goals for different patients. How do patient preferences, frailty, comorbidities, and quality-of-life considerations shape your treatment decisions?**

I don't know if it affects initial treatment as much as it affects second- and third-line therapies. I think that's where individualized decision-making is so important. We've got bispecific antibodies, we've got CAR-T [chimeric antigen receptor T-cell therapy], we've got Tafa-Len [tafasitamab plus lenalidomide]. Those all have different risks, different needs for hospitalization, different dosing schedules. But for the time being, most treatment for upfront large cell lymphoma is going to be once–every-3-week chemotherapy. It's going to be given in the outpatient setting for most people. It's going to be given with growth factor. Maybe there's going to be some difference in how rituximab or the growth factor is administered. But for most people upfront, it's going to end up looking relatively similar. It might just be more about the dose intensity of treatment. If we ever have to avoid anthracycline, that gets more complicated. The regimens where we take out the Adriamycin and put something else in have more complicated dosing schedules. Occasionally, you do have a patient who doesn't want chemotherapy. In shared decision-making, you work with them to figure out the next best thing that is reasonable for them.

**As more therapies move into earlier lines of treatment, how much are you thinking about preserving future options when choosing first-line therapy?**

I think this is going to be a big conversation with the frontMIND data. In that trial, R-CHOP was randomized against tafasitamab, which is anti-CD19, and lenalidomide. It did improve progression-free survival over R-CHOP backbone, but it was a fairly toxic regimen in this particular trial, which I think has made people not as excited as you might think we would be for a regimen that shows a progression-free survival advantage. Another worry about that regimen is if you do give several doses of an anti-CD19 and they happen to be in the unfortunate minority of people who relapsed early, are you potentially going to affect your CAR-T effectiveness if that's where you're going to go for your next line of therapy? For the CD19-directed therapies, it's a real concern.

As we move into an era where we might give a CD3, CD20 bispecific up front, there's maybe slightly less of a concern, at least for the next line of therapy. You're probably going to CAR-T, but then you have a different concern there. It's less about CD19, CD20 and losing antigen, but there's this worry that if you already used a T-cell–engaging therapy, what if there's something about that person's tumor where there's not particularly sensitive to T cells going after it? It's less about the antigens you're hitting and more about the fact that just T-cell–directed therapy isn't going to be the next best choice for that particular person.

I think there are going to be a lot of the same conversations we already have about therapy sequencing. There's just going to be a little bit of a twist on it, and there's a risk-benefit of this. If it turns out that these newer regimens end up putting more people in remission, and fewer people need to get those second-line therapies, then that's probably a risk we're going to end up taking, knowing that second- or third-line treatment is going to be more complicated or [we will] have to be more thoughtful than what we would currently do today.

# New Data Clarify Cardiovascular Risks of HMA and Venetoclax in AML

*By **Nichole Tucker***

Major adverse cardiovascular events (MACE) occur frequently and early in patients with acute myeloid leukemia (AML) treated with venetoclax and hypomethylating agents (HMA), according to a multicenter cohort study. The findings suggest MACE is associated with worse survival outcomes.

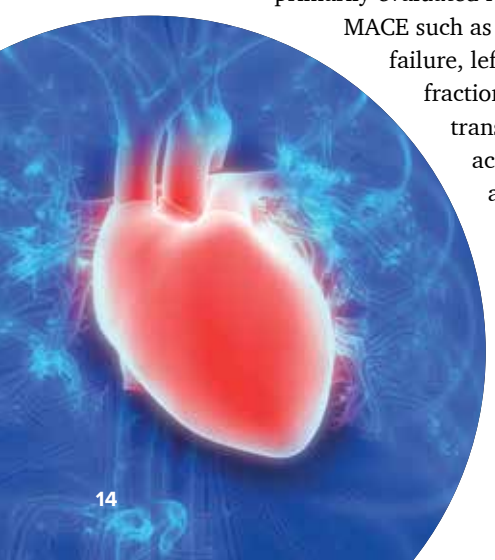
Lead investigator **Marielle Scherrer-Crosbie, MD, PhD,** of the Hospital of the University of Pennsylvania, explained what these findings reveal about the cardiovascular vulnerability of patients with AML receiving HMA and venetoclax.

Marielle Scherrer-Crosbie, MD, PhD

"There may be several factors involved: the patients with AML treated with HMA-venetoclax are older, have a substantial burden of cardiovascular risk factors that are associated with the development of these complications, and some have pre-existing cardiovascular diseases," she said.

Considering average age and number of comorbidities in the population of patients with AML, defining MACE in this group is important. Thus, study investigators from six healthcare systems sought to characterize the incidence, phenotypes, predictors, and prognostic implications of MACE in patients with AML, resulting in the largest multicenter retrospective cohort study of its kind.

The study included 1,012 adult patients with a mean age of 69 ± 12.5 years. The population was largely male (57%), and all patients had newly diagnosed or relapsed or refractory AML treated with HMA and venetoclax. Patients were primarily evaluated for the occurrence of MACE such as atrial fibrillation, heart failure, left ventricular ejection fraction reduction, stroke/transient ischemic attack, acute coronary syndrome, angina, ventricular tachycardia/fibrillation, myocarditis, or cardiovascular death. The secondary end point explored in the study was noncardiac mortality.



According to the published results, 200 patients (20%) experienced MACE. The median time to first MACE was 120 days and a 12-month cumulative incidence of 17%. The most frequent events observed were atrial fibrillation (6%), stroke/transient ischemic attack (5%), left ventricular ejection fraction reduction (5%), and heart failure (4%). In total, 282 cardiovascular events occurred over a median follow-up period of 280 days (interquartile range: 98-580; range 2-2,615 days).

Patients with diabetes had a significantly higher risk of MACE, with diabetes independently predicting these events (subdistribution hazard ratio [HR], 1.4; 95% CI, 1.03-1.89; $P=0.031$). Moreover, a correlation was observed between the incidence of MACE and increased mortality (73% vs 56%; HR, 1.96; 95%; CI, 1.59-2.42; $P<0.001$), as well as treatment disruption.

"The early period of AML treatment is associated with numerous cardiovascular stressors and often large variations in blood volume that can precipitate events. Finally, in animal studies, venetoclax has been reported to induce myocardial injury, mediated by oxidative stress and apoptosis, and may contribute to these complications," said Dr. Scherrer-Crosbie.

According to Dr. Scherrer-Crosbie and colleagues, patients with AML who receive HMA and venetoclax require close monitoring for cardiovascular events, and early intervention is warranted for those with cardiometabolic risk factors like diabetes.

"It is crucial that hematologists and cardiologists work together so that the AML treatments can be administered seamlessly and without complications. Patients who have a high risk of cardiovascular complications can be identified before treatment by their baseline demographics, cardiovascular and cancer history, and clinical/laboratory characteristics. Involvement of cardio-oncology at this stage is helpful for further cardiovascular assessment, risk factor identification and management, and close monitoring of the patients to limit the occurrence of these complications," she advised.

**REFERENCE:**

Filimon S, et al. *JACC Adv.* 2026 Jun;5(6 Pt 2):102821. doi: 10.1016/j.jacadv.2026.102821

PHOTO CREDIT: iSTOCK.COM/MAGICMINE

## Talquetamab Doublets Improve Survival in Relapsed or Refractory Multiple Myeloma

*By **Melissa Badamo***

Talquetamab in combination with teclistamab or pomalidomide delivered statistically significant and clinically meaningful survival improvements in patients with relapsed or refractory multiple myeloma, according to updated results of the MonumenTAL-6 trial announced in a press release by Johnson & Johnson.[1]

The phase 3, three-arm trial compared teclistamab plus talquetamab or talquetamab plus pomalidomide with investigator's choice of elotuzumab, pomalidomide, and dexamethasone (EPd) or pomalidomide, bortezomib, and dexamethasone (PVd) in adult patients who had received one to four prior lines of therapy, including lenalidomide and an anti-CD38 antibody.[1]

Jeffrey Matous, MD

"The combination of talquetamab and teclistamab has been explored in the RedirecTT-1 studies, demonstrating response rates comparable to CAR [chimeric antigen receptor] T-cell therapy and very high response rates in extramedullary disease," **Jeffrey Matous, MD,** a member physician at the Colorado Blood Cancer Institute and investigator of the preliminary MonumenTAL-2 trial, told *Blood Cancers Today*. "The rationale is primarily through dual targeting of both the BCMA and GPRC5D antigens."

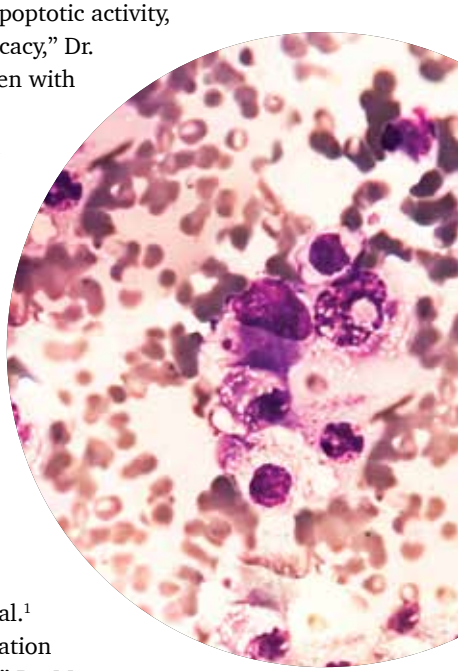
Teclistamab plus talquetamab yielded the most benefit for these patients, showing the synergistic effects of combining two bispecific antibodies. This doublet reduced the risk for disease progression or death by 89% compared with the standard of care, with the lowest hazard ratio (HR) observed in a phase 3 study of bispecific antibodies in relapsed or refractory myeloma (HR, 0.11; 95% CI, 0.08-0.16; $P<0.0001$). Talquetamab plus pomalidomide reduced the risk of progression or death by 73% compared with the standard of care (HR, 0.27; 95% CI, 0.2-0.35).[1]

"This study demonstrates the power and benefit of immunotherapy doublets over what are now antiquated regimens," Dr. Matous said. "Until these T-cell engager combinations are incorporated into frontline treatment, which is in my opinion inevitable, they will be of paramount importance in treating both early and late relapsed disease."

Both investigational arms met the primary end point of progression-free survival (PFS) and demonstrated a safety profile comparable with known adverse events of each drug.[1] In a phase 1b-2 trial, grade 3 or 4 infections occurred in 64% of patients who received talquetamab plus teclistamab, a higher rate than observed with either agent administered as monotherapy.[2] Teclistamab contains a safety warning for cytokine release syndrome and immune effector cell–associated neurotoxicity syndrome.[1]

Preliminary data from MonumenTAL-2 showed that talquetamab plus pomalidomide yielded high, deep, and durable responses in patients with relapsed or refractory multiple myeloma, supporting the phase 3 MonumenTAL-6 study. The combination demonstrated a median PFS of 25.8 months, a 12-month PFS rate of 72.6%, and an overall response rate of 85.7%. The median duration of response was not reached.[3]

"In the example of pomalidomide combinations, we know from the phase 1b MonumenTAL-2 study that combining pomalidomide, which is a very active immunomodulatory drug with direct on-tumor apoptotic activity, could lead to synergistic efficacy," Dr. Matous added. "This was seen with quite high response rates in that study in patients with a median of three prior lines of therapy."



The full results of the phase 3 MonumenTAL-6 study will be presented at a future medical conference, according to Johnson & Johnson. The study's secondary end points are overall response rate, complete response or better, measurable residual disease–negative complete response, and overall survival.[1]

"I really like the fixed duration therapy of these treatments," Dr. Matous concluded. "I will be looking for durability of the responses and updated information regarding the on-target, off-tumor side effects of targeting GPRC5D."

PHOTO CREDIT: iSTOCK.COM/MD ARIFUL ISLAM

**REFERENCES:**


1. PR NewsWire. Accessed July 27, 2026. https://www.prnewswire.com/news-releases/tecvayli–talvey-reduced-the-risk-of-disease-progression-or-death-by-89-and-the-risk-of-death-by-62-in-earlier-line-relapsedrefractory-multiple-myeloma-302833309.html
2. Cohen YC, et al. *N Engl J Med.* 2025;392(2):138-149. doi:1056/NEJMoa2406536
3. 68th American Society of Hematology Annual Meeting & Exposition. Abstract No. 2282.

## Prior Authorization Delays Add Complexity to Medication Access and Treatment Decisions

*By **Rebecca Araujo***

An analysis in *JAMA Health Forum* highlights the real-world impact of prior authorization (PA) barriers, showing that patients prescribed branded medications often experienced delays in starting treatment after coverage denials or approval challenges. The study identified medication as well as prescriber and patient characteristics associated with higher rates of treatment disruption.

### Disruptions in Access

Yang Wang, PhD

The research team, led by **Yang Wang, PhD,** of Johns Hopkins Bloomberg School of Medicine, analyzed a nationwide sample of outpatient pharmacy claims data from 2024. They focused on branded medications with no existing generic version.

In total, more than 205,000 branded medication dispensations faced initial PA rejection, impacting more than 156,000 patients. Of these initial rejections, 35% were processed in 1 day. The remaining patients experienced a median authorization processing delay of 6 days, after which point only 54% were eventually approved. Around one-quarter of denied claims were denied within 1 day, and 19% were denied after multiple days.

"This empirical evidence demonstrated the frequent treatment delays and denials caused by PA, adding to a growing body of literature on the impact of PA on curbing treatment access," the authors wrote.

### Delays and Denials

Factors such as claim adjudication complexity and prescription characteristics were associated with likelihood of adjudication delays and eventual denials. For example, prescriptions with supplies exceeding 30 days had 4% lower approval rates.

Same-day adjudication was less likely for prescriptions that required multiple rounds of PA, those with multiple rejection reasons, and refills. However, prescriptions with additional rejection reasons and refills had a higher likelihood of eventual approval.

"For PA cases with high probability of eventual approval, alleviating PA requirements would not only improve patients' timely access to medications but also reduce insurers' financial cost and increase their administrative efficiency," the authors recommended.

### Who Faces More Barriers?

Prescriptions from clinicians with a corporate affiliation had a 3% higher approval rate than those coming from independent practitioners. "This may be associated with better access to resources that help clinicians navigate the PA requirements and assist with prescribing decisions," the authors noted.

Patient factors were also associated with authorization timing. For instance, patients with multiple conditions had a 5% lower approval rate. Compared with Medicare insurance, patients with Medicaid insurance had an 8% lower approval rates.

"Our results suggest greater PA-related access frictions at pharmacy counters for patients with greater and more complex health needs and with fewer socioeconomic resources—potential negative implications for treatment outcomes," the authors cautioned.

Dr. Yang and colleagues closed by noting that, although their findings can "inform patients and clinicians regarding the dynamics and nuances of the PA process," they hope that these data can also lead to payer-led improvements in the PA process to improve treatment access.

**REFERENCE:**

Wang Y, et al. *JAMA Health Forum.* 2026;7(4):e260760. doi:10.1001/jamahealthforum.2026.0760



PHOTO CREDIT: iSTOCK.COM/SDI PRODUCTIONS

# Editor's Picks

*In each issue of* Blood Cancers Today (BCT), *we will take a closer look at a particular topic in hematologic malignancies. This month,* BCT *Editor-in-Chief* ***Krina K. Patel, MD, MSc,*** *Associate Professor, Department of Lymphoma Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, highlights the latest multiple myeloma research.*

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

Krina K. Patel, MD, MSc

**MULTIPLE MYELOMA**

## Cevostamab Draws Durable Responses in Myeloma After BCMA CAR-T Failure

*By* ***Dean Patterson***

Cevostamab elicited response in 43.9% of patients after failure of B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T-cell therapy, and those responses held for a median of 17.4 months, according to new data.

**Shaji Kumar, MD,** of Mayo Clinic, presented the pooled exploratory and expansion cohorts of the phase 1/2 CAMMA 2 study at the 2026 European Hematology Association Annual Meeting.

Shaji Kumar, MD

"This is very meaningful. The post-CAR T next line of therapy PFS [progression-free survival] has been approximately 6 months in the different studies. This represents an important and clinically relevant improvement," he told *Blood Cancers Today.*

Cevostamab is a first-in-class bispecific antibody against FcRH5, a type I membrane protein found on myeloma cells regardless of BCMA status. All 41 patients in the analysis had received BCMA-targeted CAR T; three-quarters of them received it as their most recent line of treatment at a median of 13.4 months before enrollment. The median age was 66 years, and the median number of prior treatment lines was five. Every patient had triple-class refractory disease, 43.9% had penta-drug refractory disease, and 16 of 26 evaluable patients had high-risk cytogenetics.

By the January 30, 2026, cutoff, 34.1% of patients had reached a very good partial response (VGPR) or better, and 19.5% had a stringent complete response. Median duration of response was 17.4 months (95% CI, 9.0-not estimable); eight of 18 responders were still in remission, and 59.8% of responses were intact at 15 months. Median duration of study treatment was 12.9 months.

Toxicity tracked what clinicians already expect from T-cell engagers. Cytokine release syndrome (CRS) was observed in 75.6% of patients but never exceeded grade 2, and three-quarters of events showed up within a day of ending the infusion. When CRS occurred, management frequently consisted of tocilizumab or steroids, and all CRS events were resolved. Infections of grade 3 or 4 were noted in 39% of patients, and just over half of the cohort needed immunoglobulin supplementation. Cytopenias were frequent and often grade 3 or 4, with neutropenia at 51.2% and anemia at 31.7%, although no patients died. Two deaths, one due to pneumonia and one due to myelodysplastic syndrome, were judged to be unrelated to treatment. One patient stopped treatment because of an adverse event.

Dr. Kumar stated, "The drug was very well tolerated, with adverse events comparable to what we see with bispecifics in general."

The correlative data explain why the approach works in patients who have exhausted BCMA-targeted treatment. In screening marrow aspirates, FcRH5 was detected on a median 83.1% of malignant plasma cells, and GPRC5D on 72.4%. BCMA was down at 14.0%. Cytokine induction and rising soluble CD25 followed step-up and target dosing, whereas soluble BCMA fell from the second step-up dose in patients who went on to a VGPR or better.

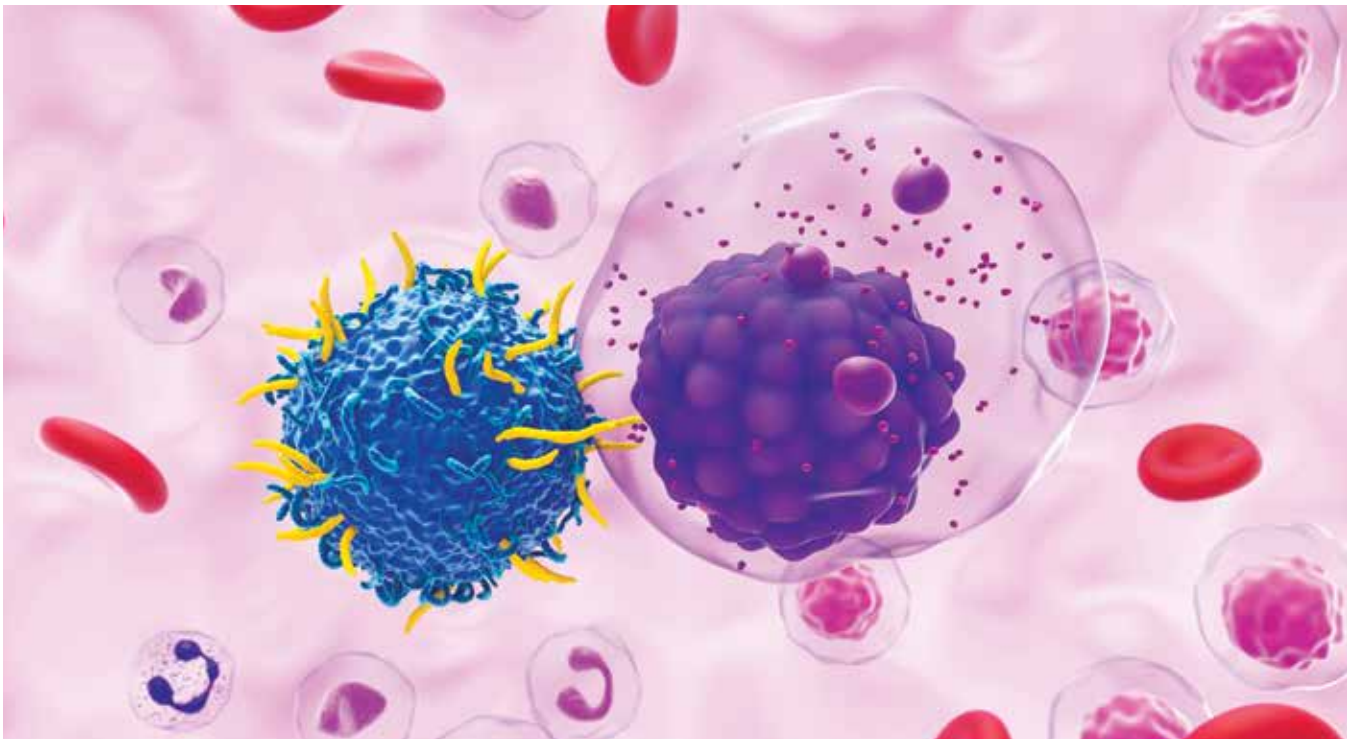
Investigators are still concerned with two questions. Does the drug still work after GPRC5D-directed therapy, or only after BCMA-targeted therapy? And does using it early in the course of treatment cost patients a later T-cell redirection? In regard to the second question, 22 of 33 eligible patients received another line, most often a GPRC5D- or BCMA-targeted bispecific, with a median of two subsequent lines.

"Larger studies, ideally prospective studies that will allow us to control the other confounding variables to delineate the activity of cevo [cevostamab] in patients relapsing after BCMA- and/or GPRC5D-targeted therapies, will define its role in the myeloma landscape," Dr. Kumar said.

CAMMA 1 arm B is testing cevostamab with pomalidomide and dexamethasone in BCMA-naive patients. Read against these results, the two trials point toward a drug that works whether BCMA has been used up.

**REFERENCE:**

2026 European Hematology Association Annual Meeting. Abstract No. PS1865.



# Impact of Disease Biology in Patients With Relapsed or Refractory Multiple Myeloma Following CAR T-Cell Therapy

*By* ***Lauren Evoy Davis***

As new treatments are developed, studied, and tested, researchers are trying to figure out how to improve outcomes in patients with relapsed or refractory multiple myeloma (RRMM). RRMM is defined as a progressive disease, poor response despite treatment, progression within 60 days of the most recent treatment in a patient who was in remission, the absence of at least minimal response, or primary refractory multiple myeloma, according to the NIH.

Investigators evaluated various bridging strategies after B-cell maturation antigen-directed CAR-T cell therapy in patients with RRMM to see how disease biology affected outcomes and response prior to CAR-T cell infusion.

The study included 90 patients with RRMM at several cancer centers in Austria who received CAR-T cells between January 2024 and July 2025. Of the 90 patients, 47.8% received idecabtagene vicleucel and 52.2% received ciltacabtagene autoleucel as part of the CAR-T cell infusion.

The investigators extracted clinical and treatment-related data from electronic health records, including baseline characteristics, cytogenetic risk, prior therapies, holding and bridging therapy, which can include therapy before and after T-cell apheresis (the collection of white blood cells used to create the CAR-T cell therapy).

At a median follow-up of 9.9 months, the estimated median progression-free survival (PFS) was 17.1 months.

In another model, investigators observed that some patients experienced a good partial response prior to CAR-T infusion, which was associated with a trend toward improved PFS but was not considered statistically significant.

The investigators concluded that the unfavorable outcomes after intensive bridging were driven by adverse baseline disease characteristics, not treatment-related effects.

These findings suggest that inferior outcomes observed after intensive bridging are largely driven by adverse baseline disease characteristics rather than treatment-related effects. Helping patients control disease before CAR-T infusion is crucial to improving outcomes.

**REFERENCES:**

1. Ahmed A, et al. *StatPearls.* Treasure Island (FL): StatPearls Publishing; June 8, 2023.
2. Strassl I, et al. *Transplant Cell Ther.* Published online July 2, 2026. doi:10.1016/j.jtct.2026.06.048

PHOTO CREDIT: iSTOCK.COM/NEMES LASZLO

# Cemsidomide Shows Encouraging Results for Patients With Advanced Myeloma

*By* ***Leslie Feldman***

Cemsidomide, an experimental oral drug, has shown promising results for patients with relapsed or refractory multiple myeloma (RRMM) whose cancer has returned after multiple treatments, offering another treatment for a patient population with few remaining options.

Sagar Lonial, MD

In June, lead investigator **Sagar Lonial, MD,** of Winship Cancer Institute at Emory University School of Medicine, and colleagues presented updated findings from an early-stage clinical trial at the European Hematology Association (EHA) 2026 Congress. The study evaluated cemsidomide in combination with the steroid dexamethasone in patients with RRMM.

The trial enrolled 73 patients whose disease had already been treated with a median of seven previous therapies. More than three-quarters had previously received advanced treatments such as chimeric antigen receptor (CAR) T-cell therapy or bispecific antibodies, making this one of the most heavily pretreated groups of patients studied.

Researchers found that 36% of patients experienced an overall response. At the highest dose tested, the response rate increased to 53%, meaning that more than half of patients benefited from treatment. In addition, half of all participants experienced at least some degree of disease improvement or stabilization.

The most frequent serious complication was neutropenia, which occurred in 58% of patients. Serious infections were reported in 30% of participants; anemia and low platelet counts were also observed. Most cases of severe neutropenia occurred during the first two treatment cycles and were generally managed with supportive therapy such as injections of granulocyte colony-stimulating factor. Only four patients required a dose reduction because of side effects, and only four discontinued treatment due to adverse events. None of the side effects or adverse events were considered directly related to the treatment.

Researchers also reported that patients were able to continue treatment at nearly the full intended dose throughout the study, suggesting that the adverse effect of myelosuppression was generally manageable.

Although these findings are encouraging, experts caution that this was a phase 1 clinical trial designed primarily to evaluate safety and determine the best dose rather than prove effectiveness. Larger studies will be needed to confirm whether cemsidomide improves survival or delays disease progression compared with existing treatments.

Those studies are already underway. A phase 2 trial is now evaluating cemsidomide in a larger group of patients with RRMM, and another study is testing the drug in combination with elranatamab.

If future trials confirm these early results, cemsidomide could become an important new treatment option for people with multiple myeloma whose disease has progressed despite today's most advanced therapies, according to Dr. Lonial and colleagues.

**REFERENCE:**

2026 EHA Congress. Abstract No. PF763.

# HemOnc Happenings

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

## Jorge Cortes, MD, Appointed Chief of Hematology at University of Alabama

*By **Sara Karlovitch***

Jorge Cortes, MD

**Jorge Cortes, MD,** a leukemia specialist, was appointed Chief of Hematology at the University of Alabama Birmingham (UAB) and Deputy Director of the UAB O'Neal Comprehensive Cancer Center.[1,2]

Dr. Cortes previously served as director of the Georgia Cancer Center at Augusta University from 2019 to 2026. In that role, he managed the center's effort toward an NCI designation, which is ongoing.

"O'Neal Cancer Center is one of the initial NCI Designated Cancer Centers and is one that truly represents what NCI designation represents, using science and research for the good of the community all over Alabama and beyond. I am honored to be part of this mission," Dr. Cortes said in an interview.

Outside his leadership roles, Dr. Cortes has a storied research career, having received more than 230 grants and contracts as a principal investigator. His research has led to FDA approval of four leukemia drugs: bosutinib, ponatinib, omacetaxine, and glasdegib. He was also active in the development of CPX-351, gilteritinib, quizartinib, and crenolanib.[3]

His research background has equipped him to help the O'Neal Comprehensive Cancer Center to translate trial data and results into clinical practice. "There is good clinical research at the O'Neal Cancer Center, but there is tremendous potential to grow it even further. There is excellent basic research, outstanding resources, and a large body of faculty that are very good in their fields. My job is to help bring all elements together to further enhance the translational research, support new initiatives, find funding, and advance science," Dr. Cortes said.

In his new role at UAB, Dr. Cortes hopes to mentor young faculty members to help them advance their careers.[4] "My main goal is to support the excellent faculty we have in the division to thrive and develop their careers," Dr. Cortes stated. "We have many talented faculty, many of them early in their careers. I aim to be a mentor to them, provide them the resources to do their research and clinical activities, and promote them in their career advancement."

**REFERENCES:**


1. O'Neal Comprehensive Cancer Center. Accessed June 10, 2026.
2. O'Neal Comprehensive Cancer Center. Accessed June 10, 2026.
3. Augusta University. Accessed June 10, 2026.
4. The University of Alabama at Birmingham. Accessed June 10, 2026.


## Tycel Phillips, MD, Recognized for Lymphoma Excellence

*By **Melissa Badamo***

Tycel Phillips, MD

**Tycel Phillips, MD,** associate professor in the Division of Lymphoma at the Department of Hematology & Hematopoietic Cell Transplantation at City of Hope, received the James O. Armitage Lymphoma Clinical Investigator Award at the Pan Pacific Lymphoma Conference (PPLC) for his commitment, excellence, and innovation in lymphoma research.[1]

With expertise in B-cell lymphomas such as chronic lymphocytic leukemia, mantle cell lymphoma (MCL), and diffuse large B-cell lymphoma, Dr. Phillips served as the principal investigator of several groundbreaking clinical trials.[2] He has led pivotal research on the bispecific antibody glofitamab in patients with relapsed or refractory MCL, showing that the fixed-duration regimen produced durable complete responses with manageable safety.[3]

The award is named after **James O. Armitage, MD,** a professor in the University of Nebraska Medical Center (UNMC) Division of Hematology, who is credited for pioneering their bone marrow transplantation program.[4]

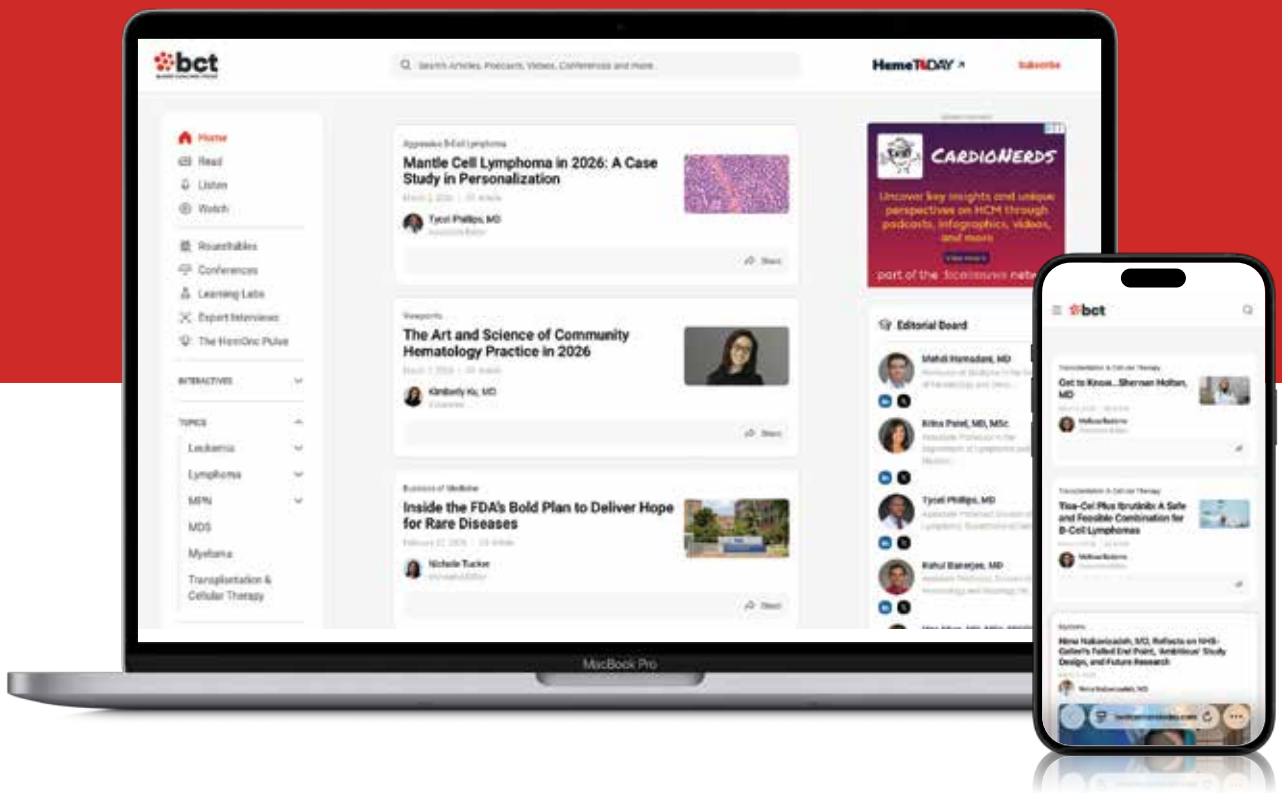
"The James O. Armitage Lymphoma Clinical Investigator Award is a great honor bestowed upon a 'young' clinical investigator at the PPLC meeting committee. The award to me is validation of the impact of mentorship on junior faculty and fellows," Dr. Phillips told *Blood Cancers Today.* He received the award from **Matthew Lunning, DO,** interim chief and professor in the UNMC Division of Hematology.

"I personally owe this award to several physicians who have greatly impacted my career," Dr. Phillips continued. "These include Drs. Paul Barr and Brenda Cooper while I was a fellow and Dr. Moshe Talpaz, who significantly helped boost my clinical research career at the University of Michigan. There are so many others who have helped me along the way, and my appreciation abounds to all of them. My family was able to see this honor, which at least gives them some perspective on the time I am away from them. Hopefully, they understand it is all in the hope of trying to improve the lives of patients that I care for."

**REFERENCES:**


1. University of Nebraska Medical Center. Accessed July 29, 2026.
2. City of Hope. Accessed July 29, 2026.
3. Phillips TJ, et al. *J Clin Oncol.* 2025;43(3):318-328. doi:10.1200/JCO.23.02470
4. Printz C. *Cancer.* 2019;125(3):329-330. doi:10.1002/cncr.31968

# BLOOD CANCERS TODAY JUST GOT BETTER.




## EXPLORE THE REDESIGN AND JOIN THE DISCUSSION WITH YOUR PEERS.

**www.bloodcancerstoday.com**

"Beautiful and intuitive—this website will really increase physicians' access to interact with their peers."

*– Dr. Anthony Petrillo*

bct
BLOOD CANCERS TODAY

figure1

# Where Clinicians Come to Collaborate

New!
Video case posts are here.

Join us as we take clinical social media to the next level!

figure1