Insider

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COVER STORY

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EDITORIAL

How to muddle through the less good times? Practice aequanimitas

By: **Amy DeZern, MD, MHS**
Professor of Oncology, Johns Hopkins University School of Medicine

Thanks to the many happy choices I have made over the years, my personal and professional lives are full and busy in 2025.

However, that doesn't mean that day-to-day life is straightforward and stress-free. I am a mother of four children (and a dog) as well as a division director for heme malignancies in my cancer center. I have to laugh sometimes when people ask me how I manage, and I usually acknowledge that "some days it's easier than others to keep all the balls in the air."

There are ups and downs for us all—personally and professionally. As my children grow up, the hurdles have also increased with harder questions for them. How will sports tryouts go? Will we survive the middle school years (again)? When do we start planning for college?

And while the ups and downs of parenting are a tale as old as time, in medicine, especially academics, it seems like we have more downs than ups as of late. Some of those hurdles are and have been ever present: Will the patient benefit from the new treatment? Will we get the next grant? Will that paper be published? But others are new, and for most of us, unprecedented. Will a hiring freeze impact growth of our division? Are all faculty members supported in a balanced fashion? Are hospitals going to weather changes in Medicare and Medicaid funding? What will happen to our cancer center in the era of changing NIH funding? And so on.

In this uncertain time, it is challenging for me, as I'm sure it is for many of you, to keep a balance between my personal and professional lives. But the truth is that there are significant parallels. Just as my children are learning to exist and (hopefully) to thrive in the world, so we in medicine are also trying to adapt and (hopefully) thrive in a rapidly changing environment. I am frequently reminded—more often than I might have thought—that many lessons transcend any particular age and setting.

As I work hard to be a better mother and division leader, I do search for and draw on messages that speak to me to muddle through the less good times. One is a mantra instilled in me since I was an intern: Aequanimitas! This was one of Sir William Osler's most famous essays, delivered to new doctors at the University of Pennsylvania School of Medicine. In the essay, Osler, one of the founding members of Johns Hopkins Hospital, advocates two qualities: "imperturbability" and "equanimity," which he defined as "coolness and presence of mind under all circumstances." This is currently not always easy for me at home or at work, but I do aspire to Osler's ideal and so repeat the mantra "Aequanimitas" to myself both at work and at home. Before I walk into a sick patient's room: "Aequanimitas." Before I meet with my administrative leadership: "Aequanimitas." Before reviewing budgets and effort and time and resources: "Aequanimitas." And yes, when I get home late, and there is homework to be done, and sports practices to attend, and dinner to make: "Aequanimitas."

There are no easy answers or solutions to the problems we face as a profession, as a specialty, and as a society. There will be hard decisions to make, and much uncertainty to face. In these fragile, stressful, and disconcerting times, I hope you all can find moments of calm, and reflection, and aequanimitas.

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2025-2026 Meeting Calendar

November 20, 2025
SOHO Breakthroughs in Blood Cancers
VIRTUAL

February 4–8, 2026
2026 Tandem Meetings
SALT LAKE CITY, UT

April 29–May 2, 2026
2026 ASPHO
MINNEAPOLIS, MN

June 11–June 14, 2026
EHA 2026 Congress
STOCKHOLM, SWEDEN

December 6–9, 2025
67th American Society of Hematology Annual Meeting and Exposition
ORLANDO, FL

February 26–28, 2026
30th Annual International Congress on Hematologic Malignancies
MIAMI BEACH, FL

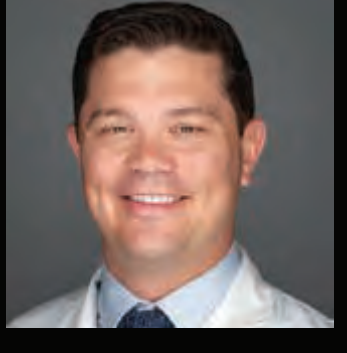
May 29–June 2, 2026
2026 ASCO Annual Meeting
CHICAGO, IL

September 9–12, 2026
14th Annual Meeting of the Society of Hematologic Oncology
HOUSTON, TX

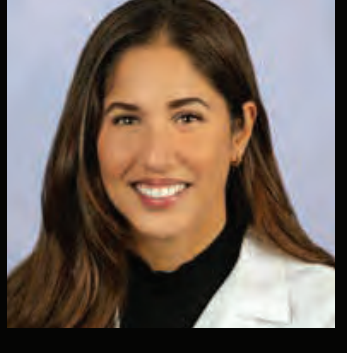
soho Insider PODCAST

Susan O'Brien

Saad Usmani



Andrew Kuykendall



Megan Melody

COVER STORY

SOHO pilot program finds structured learning improves practice in relapsed or refractory CLL/SLL

This joint initiative between SOHO and MLI was created to educate and empower early-career clinicians treating patients with R/R CLL/SLL.

By: **Karine Cohen-Solal, PhD**

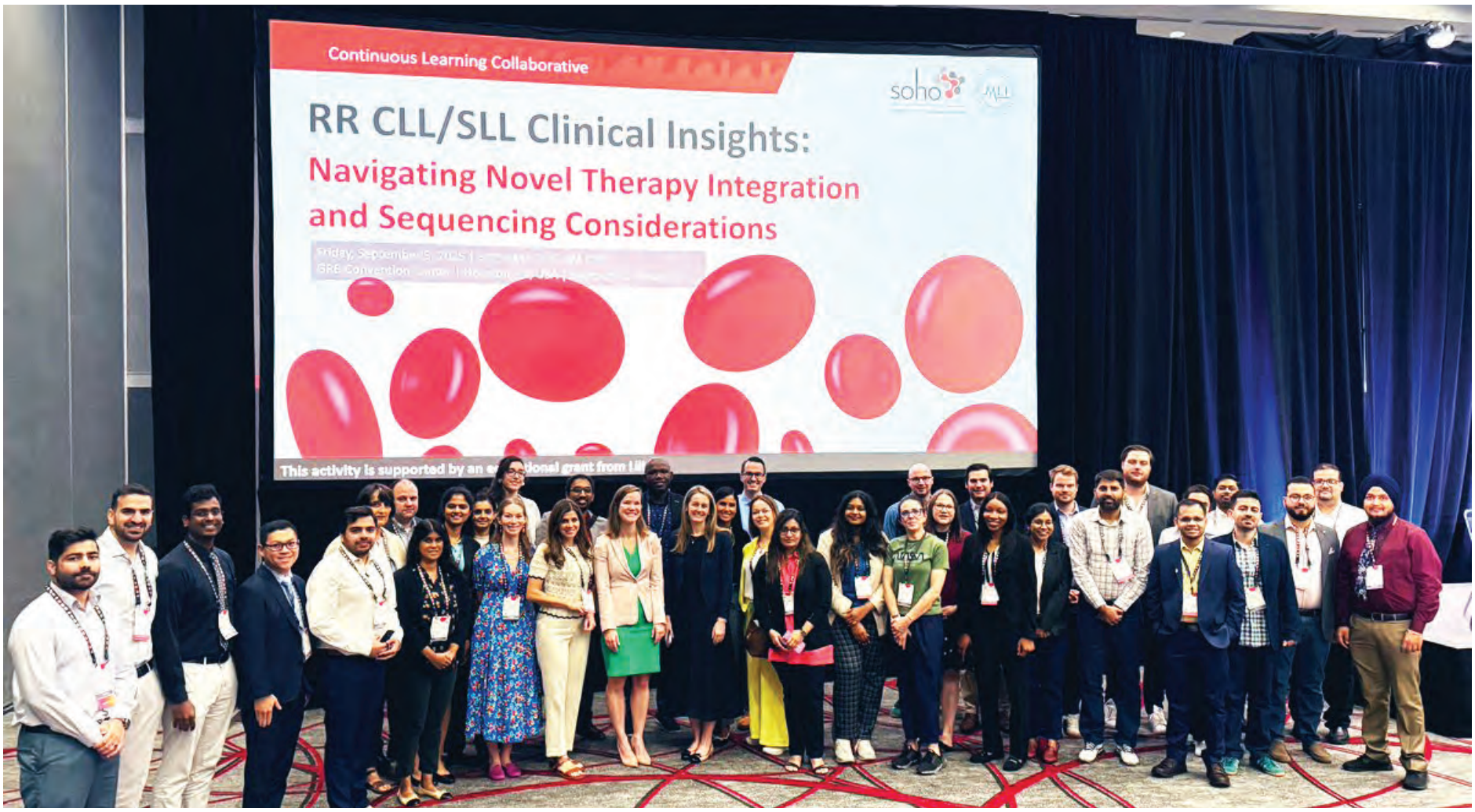
At the Thirteenth Annual Meeting of the Society of Hematologic Oncology (SOHO 2025), a new pilot program debuted to educate and empower the next generation of clinicians treating patients with relapsed or refractory (R/R) chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL).

The Continuous Learning Collaborative (CLC), titled, "R/R CLL/SLL Clinical Insights: Navigating Novel Therapy Integration and Sequencing Considerations," is a partnership between SOHO and the Medical Learning Institute (MLI) created for early-career clinicians (those within 10 years of practice) working in community or smaller academic settings.

In the first phase, insight was collected from the cohort of 25 participants during the summer of 2025. The second phase of the pilot study was intended to extend the reach of the program to clinicians with longer time in practice. That was achieved with a live intensive at SOHO 2025, which was open to all SOHO attendees, some of whom have been in practice for over 15 years.

Phase 1 structure and insights

Launched in summer 2025, the initiative engaged 25 young investigators in phase 1 to collect real-world, practice-based insights that informed the design of the subsequent live intensive. Participants contributed de-identified electronic health records (EHR) from five of their



own patients, responses to interactive case simulations via MLI's Build Your Own Case Study™ (BYOCS™) platform; and detailed surveys capturing current R/R CLL/SLL treatment patterns and approaches.

Analysis of these inputs revealed the following important trends:

- **Participants, though early in their careers, consistently ordered key prognostic tests, including del(17p), TP53, and IGHV tests. This aligns with guidelines favoring risk-adapted approaches.**
- **Acalabrutinib and venetoclax-based therapies dominated prescribing patterns (84% each), with pirtobrutinib at 48%, indicating uptake post-accelerated approval. International respondents highlighted access barriers in resource-limited settings, including Pakistan and Egypt.**
- **Participants reported atrial fibrillation (84%), bleeding (56%), and infections (56%) as being the most challenging BTKi-related adverse events (AEs) /toxicities.**
- **Most participants noted integrating patient-specific factors into treatment decisions, including preference for oral administration, time-limited duration of regimens, refusal of infusion/IV, quality of life, and convenience.**
- **Data from 116 patient records revealed a progression from ibrutinib-dominant as first-line therapy to acalabrutinib/zanubrutinib/venetoclax in second and third lines, with pirtobrutinib emerging in later lines.**
- **Growing interest in clinical trials (24% of participants) and novel modality like lisocabtagene maraleucel (8%) prescribed/selected during the last six months indicate a forward-looking approach from participants in the adoption of CAR-T and other innovative treatments.**

Participants also identified educational needs. One learner noted, "To optimize the use of BTKis, including newer agents like pirtobrutinib, the most helpful resources would include clear, clinical algorithms for treatment sequencing, especially in the context of prior BTKi exposure or resistance. Guidance on when and how to perform molecular resistance testing would be valuable, as would practical tools for managing common toxicities such as atrial fibrillation, hypertension, and bleeding."

Phase 2: live intensive at SOHO 2025

The 90-minute live session integrated phase 1 insights, allowing participants to apply the latest evidence-based guidelines to real-world patient scenarios. Activities included case-based decision-making and immediate expert feedback. Group discussions addressed AE management and sequencing challenges.

Key findings are as follows:

- **All attendees (100%) reported intent to enhance their practice via guideline adherence, evidence-based personalization, and patient-centered decision-making.**
- **All learners (100%) rated the activity highly for achieving the learning objectives, faculty expertise, engaging format, teaching and learning methods, and bias-free content. One participant commented, "It will impact not only my practice but first of all the life of the patients."**
- **Comments included incorporating evidence on adverse events, shared decision-making, and differences between BTKi-refractory and BTKi-exposed disease to help improve patient outcomes.**
- **In the preceding six months, venetoclax-containing regimens (70%) and covalent BTKis such as acalabrutinib and ibrutinib (57% each) were most frequently prescribed, followed by zanubrutinib (38%). Noncovalent BTKis (eg, pirtobrutinib; 24%) were primarily used for efficacy, based on recent evidence (19%) or prior resistance to BTKis (46%).**
- **Similarly to the data from the 25 learner-cohort from phase 1, clinical trials (27% of participants) and lisocabtagene maraleucel (8%) were selected or prescribed during the last six months, confirming a positive approach toward emerging treatment modalities and agents or regimens.**
- **Atrial fibrillation (46%) and hypertension (30%) were the most challenging BTKi-related adverse events to manage. Bleeding, neutropenia, and arthralgias/myalgias (27% each) were also frequently cited.**
- **Learners preferred noncovalent or second-generation covalent BTKis for younger or intolerant patients, venetoclax-based regimens for moderately fit or travel-oriented patients, and zanubrutinib for elderly, frail, or relapse-concerned patients.**
- **Learners identified limited access to multidisciplinary care (25%), patient adherence (20%), and systemic issues such as insurance and reimbursement (20%) as major barriers. The program provided strategies to overcome these barriers for 70% of learners.**
- **Learner questions reflected ongoing uncertainty about post-resistance therapy sequencing, management of atrial fibrillation and CNS disease, retreatment indications, and global access disparities.**

Group-based discussions during the live intensive

Each participant met one-on-one with a faculty member for 30 minutes, spending 15 minutes on adverse event management and 15 minutes on treatment sequencing. Discussions were related to the three cases in MLI's BYOCS™ activity, along with participants' clinical challenges.

Interests are listed as follows:

- **Preference for acalabrutinib versus zanubrutinib based on cardiac toxicity profiles.**
- **Rationale for shifting from ibrutinib to second-generation covalent and noncovalent BTKis.**
- **Use of obinutuzumab with BTKis for cytoreduction in high disease burden.**
- **Necessity and criteria for PJP prophylaxis in patients treated with BTKis.**
- **Concerns regarding PLCG2 mutations and their impact on potential resistance to pirtobrutinib.**
- **Criteria for identifying patients suitable for allogeneic stem cell transplantation.**
- **Exploration of triplet combinations in R/R settings.**
- **Optimal timing for incorporating obinutuzumab into venetoclax-based regimens.**
- **Availability and role of BTK-resistance mutation testing in treatment decisions.**

Conclusion

The pilot program showed that structured, multiphase learning can engage clinicians at all career stages and address real-world challenges in managing R/R CLL/SLL. Using EHR and survey data, case simulations, and expert feedback, the program reinforced evidence-based treatment sequencing, adverse event management, and patient-centered care. Early data suggest such initiatives can improve guideline adherence and patient outcomes across settings.

This article is the first of a series of three on the SOHO-MLI initiative, "R/R CLL/SLL Clinical Insights: Navigating Novel Therapy Integration and Sequencing Considerations."

About the author

Karine Cohen-Solal, PhD, is an experienced scientific and medical writer with extensive expertise in oncology, dedicated to advancing cancer care through clear, evidence-based communication and continuing medical education. Drawing on over 20 years of experience in oncology research, she combines deep scientific insight with exceptional writing skills to translate complex discoveries into meaningful narratives that inform clinical practice changes and ultimately elevate patient outcomes.

Pathways & Perspectives with Gabriela Hobbs, MD

Dr. Hobbs, MPN lead and clinical director for the Adult Leukemia Service at Massachusetts General Hospital, was born in Mexico City, and came to the US for college and her medical training. In this interview, Dr. Hobbs reflects on how a book about Louis Pasteur awakened her sense of wonder, about the connection between research and medicine, and how she balances honesty and hope in caring for patients.

Why did you decide to become a clinician?

I always knew I wanted to be a doctor. My parents had a series of children's books, and one was about Louis Pasteur and his discovery of the rabies vaccine.

A big part of that book focused on the immune system, and I thought it was amazing that Pasteur could notice something happening around him, take it to a lab, and develop a vaccine that worked through activating the immune system. I've always been fascinated by the connection between medicine and research, even if I didn't fully understand it at the time.

In 2001, when I was in college, imatinib was approved for CML, and the idea of a targeted therapy for cancer felt like exactly what medicine should be striving for. During medical school, the patients I saw with leukemia were the ones who stayed with me the most.

You make a bond with those patients, and I really found that rewarding from a physician's perspective. To add to that, throughout my training, I was able to see many medications go from bench to bedside and then see medications getting approved for patients after first using them in clinical trials. It was so rewarding to see the impact these medications made in their lives. Pursuing a career as a leukemia physician had a lot of appealing aspects; I found the intensity of the patient-doctor relationship rewarding and was excited by the amount of progress in research and the development of better targeted agents.

How do you help patients cope with their initial leukemia diagnosis?

Patients are usually completely floored when they first learn they have leukemia. These patients generally come in for something that seems trivial: they might have a fever, or bleeding from the nose or gums. The next thing they know, a leukemia doctor is telling them their white blood cell count is abnormal, and that they need to stay in the hospital for a month.

That initial interaction is so dramatic and life-altering; everyone responds differently. Some go through denial, saying they feel fine or that they can't stay in the hospital because of other obligations. But there's no time to wait. If they leave, they could die.

The first week after diagnosis is overwhelming. I often tell patients, "I know we just met, and I know none of this feels real. A few days ago, life was normal. You have to trust me to move things forward while we keep talking through it."

That first week involves countless tests: bone marrow biopsy, echocardiogram, PICC line placement, discussions about clinical trials, mutations, and treatment options. It's a flood of information, and patients and families are often in shock or denial as they try to take it all in.

I spend a lot of time talking to patients and their families, especially that first week of diagnosis. Where I think the physician is most valuable is in helping to explain what the patient can expect in the future. Some patients want all the information at once, and some will need a few conversations to process. I think it's critical to help inform the patient as much as possible to help them cope with what's ahead.

How do you balance honesty and hope when speaking with your patients?

Learning how to tell a patient they have a life-threatening diagnosis while still leaving them with hope is one of the most important skills in medicine. That's the art of medicine, and why, I think, many of us become physicians in the first place. Some people have this skill naturally, others develop it, and most of us do both.

It takes time to develop that balance. Trainees need mentors who model how to speak with patients. I learned a lot by watching others: their phrasing, tone, and empathy. After more than a decade in practice, I've grown more comfortable with that discomfort, but it never gets easy.

People may think physicians become hardened, but the longer you do this, the more you understand what lies ahead for your patients. You know what they're about to endure, and that makes it harder, not easier.

Who have been your greatest mentors?

I've had many mentors throughout my training, including attendings who were simply exceptional clinicians. During fellowship, I was especially influenced by my mentor, the late Dr. Mark Heaney. He was kind and gentle, able to walk into any room and immediately put patients at ease.

Another mentor, Dr. Miguel-Angel Perales, a BMT physician, helped calm patients and build rapport with his charismatic personality and reassuring demeanor. Everyone uses their personality differently to comfort patients and watching them taught me a lot, as I developed my own style.

How have targeted therapies changed the outlook for patients?

For CML, imatinib was the first targeted therapy for leukemia, transforming it into a chronic disease with life expectancies similar to the general population. Incredibly, imatinib was just the beginning. We now have multiple tyrosine kinase inhibitors, and many patients can discontinue treatment altogether because they remain in deep remission. Targeted therapies, both within and beyond CML, are now a standard part of leukemia care.

I'm an MPN specialist, and during my career I've seen the approval of four JAK inhibitors. The first, ruxolitinib (Jakafi), was approved in 2011, followed by three more since then. These drugs have truly impacted how we care for our patients and have helped to significantly ameliorate the debilitating symptoms associated with myelofibrosis.

We are now studying the next generation of targeted agents for MPN, so I think the next decade will be very exciting and bring excellent new therapeutic options for our patients.

How do you approach end-of-life conversations in oncology?

You can't be an oncologist treating life-threatening illness with medications that are toxic like chemotherapy without also being comfortable talking about death and dying.

Dr. Craig Moskowitz at Memorial Sloan Kettering once told me, "It's not your fault. It's not their fault they have cancer. These are the cards we were dealt. Our job is to help patients do the best they can with that situation."

My approach to end of life has changed with time. In residency, we are all focused on code status and want to know this immediately in case of a catastrophe while the patient is admitted. When you have a longitudinal relationship with a patient, you recognize that these conversations don't have to happen all at once. These conversations take time, but at the center is open, honest, and compassionate conversation.

Sometimes cancer is curable, and sometimes it isn't. When it isn't, part of our job is to talk about death and dying to prepare our patients and their family. It's important to recognize that these conversations still include hope—whether it's the hope of being pain free or the hope of dying peacefully at home. Hope doesn't have to mean cure.

> *You know what they're about to endure, and that makes it harder, not easier.*

Are you worried about funding or distrust in medicine and science?

In oncology, we are in a unique position because many pharmaceutical companies sponsor our research and fund clinical trials. So, our work isn't immediately affected by changes in administration or fluctuations in NIH funding. However, I am very concerned about the current political environment that threatens to destabilize the scientific infrastructure that has contributed to countless discoveries in medicine.

For example, as clinical investigators, we often build correlatives into trials, collecting samples that lab researchers use to study the biology behind treatment responses or resistance. While giving patients access to new therapies is the most important part of a trial, those correlatives are used to confirm hypotheses, understand the disease, or learn why a drug isn't working and how to make it better. That process depends on collaboration with lab investigators, who rely heavily on NIH funding.

The reason the US leads in drug development, scientific discovery, and medical innovation is its robust funding system for scientific research and innovation. Weakening it threatens that foundation. I am grateful that my work can continue uninterrupted at the moment. However, the current distrust in scientific research and the destabilization of the NIH is very concerning and scary. When you think about how small the NIH budget is compared to the country's budget, few things have resulted in such dramatic returns on investment. Regardless of each individual's political affiliation, we can all agree that if we get sick, we want to get the best possible care. Therefore, ensuring the US can continue to engage in the highest level of scientific research is critical so that we can continue to discover new and effective medications to help every American that needs them.

What do you do for fun?

I love spending time with my kids and husband, and I love being active. In the winter, we look forward to going skiing in Vermont, in the summer we love to bike on the Cape or go hiking. Personally, running is my favorite activity as it is a huge part of my mental health and social life.

If you had a different job, what would it be?

I would probably do something related to the environment, working on policies to fight global warming. I would focus on reducing single-use plastics by limiting or banning them, because it's not just about recycling, it's about reducing and reusing. I would also want to address food waste and waste in general.

Living or dead, who would you love to have to dinner?

Marie Curie if I had to pick a scientist. Otherwise, Barack Obama.

What's next for you?

It's an exciting time in my career, both as an MPN doctor doing clinical trials and as a leukemia clinical director. From an MPN perspective, I'm looking forward to the clinical trials that I have open, which are showing real promise, and to treating patients on those trials.

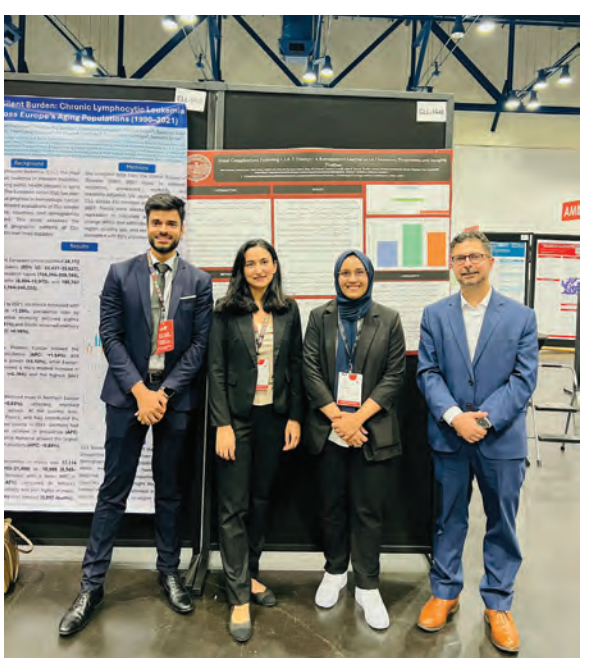
I am excited to opening several new trials that will cover the full spectrum of MPN from a trial treating JAK2 CHIP to those undergoing transplant. It's taken a long time to build a program for MPN patients where I can do this kind of work, and I feel very fortunate to be here.

From an institutional standpoint, Mass General is merging with Brigham and Women's, and our department is expanding. It has been really exciting to interview these promising new fellows who are going to become the attendings of the future. I'm so excited to have new colleagues to work with and to be part of helping the Leukemia Division of Mass General grow.

Gabriela Hobbs, MD, specializes in the care of patients with MPN and leukemias at Mass General Hospital.

Ready, Set, SOHO!

SOHO 2025 saw more than 3,000 attendees and introduced its new mascot, Killer-T. The program featured more than 1,000 poster abstracts, 160 speakers, and 180 presentations.



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Latest from the conference floor

SOHO Insider *reports from Thirteenth Annual Meeting of the Society of Hematologic Oncology (SOHO 2025)*

Bexobrutideg is well tolerated in early-phase CLL trial

Updated results from an early-phase chronic lymphocytic leukemia (CLL) trial of heavily pretreated patients showed that once-daily dosing of the Bruton's tyrosine kinase (BTK) degrader bexobrutideg was well tolerated, according to an oral abstract presented at SOHO 2025.

In this trial, 48 patients with relapsed or refractory CLL/small lymphocytic lymphoma (SLL) received six daily dose levels: 50 mg (n=3), 100 mg (n=5), 200 mg (n=9), 300 mg (n=8), 450 mg (n=7), and 600 mg (n=16). The median patient age was 68.5 years with a median of four prior lines of therapy; nearly all had prior BTKi exposure and 83% had received a BCL2 inhibitor.

Common treatment-emergent adverse events (TEAEs) were mostly low-grade, including purpura/contusion (42%), fatigue (31%), neutropenia (29% with 23% grade ≥3), rash (29%), and diarrhea (29%); there were no dose-limiting toxicities and only one discontinuation due to a TEAE.

Among 47 response-evaluable patients, the overall response rate was 80.9% (all partial responses), with a median time to first response of 1.9 months and a median duration of response not yet reached; durable responses beyond 12–18 months occurred regardless of prior therapies, high-risk mutations (TP53, BTK, PLCG2, BCL2), or central nervous system involvement.

"Bexobrutideg was well tolerated in patients, including those with longer treatment durations and higher doses," the authors wrote.

REFERENCE

Omer Z, Danilov A, Forconi F. Bexobrutideg (NX-5948), a novel Bruton's tyrosine kinase degrader, demonstrates rapid and durable clinical responses in relapsed/refractory chronic Lymphocytic leukemia: updated findings from an ongoing phase 1a study. Abstract# CLL-563. Presented at the Thirteenth Annual Meeting of the Society of Hematologic Oncology (SOHO 2025); September 3-6, 2025; Houston, Texas.

Off-the-shelf trispecific antibody has potential to shift myeloma treatment paradigm

An ongoing phase 1 study observed an 86% ORR in patients with multiple myeloma (MM) treated with the novel trispecific antibody JNJ-5322.

The study was presented by Hans Lee, MD, director of myeloma research at the Sarah Cannon Research Institute in Nashville, Tennessee, as part of SOHO 2025.

JNJ-5322 is a trispecific antibody targeting B-cell maturation antigen (BCMA) and GPRC5D via T-cell redirection.

As of January 15, 2025, 126 patients (median age, 65 years) received JNJ-5322. Patients had received a median of four prior lines of therapy, and all were triple-class-exposed; 23% received prior anti-BCMA or -GPRC5D therapy.

Patients received escalating fixed doses of JNJ-5322 ranging from 0.4 mg to 300 mg subcutaneously every two or four weeks. Patients received one step-up dose of 5 mg prior to the recommended phase 2 dose (RP2D).

Researchers determined the RP2D was 100 mg every four weeks. Almost all patients (99%) experienced one or more adverse events, the most common of which were the following: cytokine release syndrome (59%); nail-related adverse events (56%); taste-related adverse events (56%); neutropenia (48%); and nonrash skin-related adverse events (47%).

Dr. Lee presenting at SOHO 2025.

Most patients (75%) experienced infections, and 2% experienced immune effector cell-associated neurotoxicity syndrome. Four adverse event-related deaths occurred.

The ORR was 100% among patients treated with the RP2D who had not previously received an anti-BCMA or -GPRC5D therapy (n=27); response was ongoing in all of these patients at a median follow-up of 8.5 months. The median time to first response was 1.2 months.

"J&J-5322 may represent a potential paradigm shift with an overall response rate comparable to CAR-T, with manageable safety and tolerability with a convenient, off-the-shelf, every four-week dosing, with a single step-up dose to facilitate outpatient dosing," Dr. Lee said during the presentation.

REFERENCE

Lee H, Popat R, Touzeau C, et al. First-in-human study of JNJ-79635322 (JNJ-5322), a novel, next-generation trispecific antibody, in patients with relapsed/refractory multiple myeloma: initial phase 1 results. Presented at the Society of Hematologic Oncology 2025 Annual Meeting; September 3-6, 2025; Houston, Texas.

GLP-1a therapy tied to better survival, fewer complications in PV

Patients with polycythemia vera (PV) who received GLP-1a therapy had markedly better outcomes than patients who did not, according to a retrospective study presented at SOHO 2025.

"GLP-1a therapy in patients with PV was associated with significantly reduced risks of all-cause mortality, myelofibrosis, VTE, and healthcare utilization," wrote the authors. The study was led and presented by Asfand Yar Cheema, MD.

Dr. Cheema was awarded second place for top abstracts during the awards ceremony at the meeting.

Using the TriNetX database, Dr. Cheema and colleagues identified patients diagnosed with PV between 2010 and 2022 and compared those treated with a GLP-1a therapy

Dr. Cheema's study was awarded second place for best abstract at SOHO 2025.

to matched controls. A 1:1 propensity-score match balanced demographics, comorbidities, laboratory parameters, and use of cardiovascular medications that could influence mortality, according to Dr. Cheema in an interview with *SOHO Insider*.

Patients were followed for three years from diagnosis and treatment initiation to evaluate survival and key complications.

"At the end of the three years, we found a very promising

result: patients on GLP-1 receptor agonists had lower odds of all-cause mortality, progression to myelofibrosis, venous thromboembolism, acute kidney injury, and hospitalizations compared with those who were not," Dr Cheema said.

After propensity-score matching, 4,119 pairs of patients were analyzed. The investigators found that treatment with a GLP-1a therapy was linked to significantly lower odds of all-cause mortality, progression to myelofibrosis, and venous thromboembolism. Those patients also had reduced odds of hospitalization, ICU admission, acute kidney injury, and ischemic stroke or TIA.

"These findings suggest GLP-1a has therapeutic benefits for this high-risk population, requiring urgent randomized controlled trials to confirm GLP-1a efficacy and safety in PV," Dr. Cheema and colleagues wrote.

REFERENCE

Cheema AY, Munir Mishaal, Mandala A. Glucagon-like peptide-1 agonists and clinical outcomes in polycythemia vera: a large-scale propensity-matched cohort study. Abstract #MPN 642. Presented at the Society of Hematologic Oncology 2025 Annual Meeting; September 3-6, 2025; Houston, Texas.

VERONA phase 3 trial shows no survival benefit in high-risk MDS

The phase 3 VERONA trial did not meet its primary endpoint of overall survival in patients with high-risk myelodysplastic syndromes, according to an oral abstract presented at SOHO 2025.

The study, presented by Guillermo Garcia-Manero, MD, interim chair of the Department of Leukemia at the University of Texas MD Anderson Cancer Center, evaluated the efficacy and safety of venetoclax in combination with azacitidine in treatment-naive patients with high-risk MDS. The global, double-blind trial enrolled

Guillermo Garcia-Manero presents the VERONA trial at SOHO 2025.

509 patients randomized 1:1 to receive venetoclax plus azacitidine or azacitidine with placebo.

"The addition of venetoclax to azacitidine did not have an impact on overall survival in this population," Dr. Garcia-Manero said. "However, response rates were higher with the combination."

Median overall survival was approximately 22 months in both arms, but the venetoclax group achieved higher overall response rates, particularly among patients with more than 5% blasts. The regimen was well tolerated, with no new safety signals or increase in early mortality.

"This is a very important study," Dr. Garcia-Manero added. "It shows that the combination can be delivered safely worldwide, but we need to better understand which patients benefit most."

In an interview with Hagop Kantarjian, MD, Dr. Garcia-Manero said that even though the study was negative, there is still a role for venetoclax.

"Although the study may be negative, I think we're making overall progress," Dr. Garcia-Manero said. "I still believe that … venetoclax has a role for a subset of these patients."

The abstract was also awarded first place in this year's SOHO's annual abstract awards.

REFERENCE

Garcia-Manero G, Platzbecker U, Fenaux P. The primary analysis of the randomized, phase 3 VERONA study of venetoclax with azacitidine in patients with treatment-naïve, intermediate and higher-risk myelodysplastic syndromes. Presented at the Society of Hematologic Oncology 2025 Annual Meeting; September 3-6, 2025; Houston, Texas.

SOHO Insider *reports from the 2025 International Myeloma Society (IMS) Annual Meeting held in Toronto*

Daratumumab raises early infection risk in myeloma

Daratumumab raises early infection risks in patients treated with multiple myeloma (MM), according to an oral abstract presented on September 17, 2025, at the IMS Annual Meeting.

The study, which was reported as the first and largest meta-analysis to characterize the risk of infection over time in patients with myeloma receiving novel therapies, was led and presented by Alissa Visram, MD, an assistant professor at the Juravinski Cancer Center in Hamilton, Ontario, Canada.

In an individual patient-level meta-analysis of six randomized trials with roughly 3,000 participants (1,500 daratumumab patients; 1,489 nondaratumumab patients) 79% of daratumumab-treated patients developed an infection within two years (versus 61% without daratumumab), and nearly 30% experienced a serious grade ≥3 infection. Rates plateaued after six months but remained higher with daratumumab, she reported.

"Irrespective of treatment, the infection risk is highest within the first three months of therapy," she said. "However, the rates of overall and serious infections were statistically higher in daratumumab-treated patients."

After approximately six months the risk plateaued in both groups of patients, she explained, yet "daratumumab patients continued to have a higher long-term infection risk," adding that these later infections were grade 1 or 2.

"These findings provide a basis upon which to design infection mitigation strategies compatible with modern treatment regimens," she concluded during the presentation.

REFERENCE

Visram, A. Temporal trends in infectious risk among multiple myeloma patients treated with daratumumab: a meta-analysis. Abstract AO-20. Presented at the 2025 International Myeloma Society Annual Meeting; September 17-20; Toronto, Canada.

Linvoseltamab shows strong 1st results in high-risk smoldering MM

Linvoseltamab demonstrated strong early activity and a more favorable safety profile in patients with high-risk smoldering MM compared with relapsed or refractory MM, according to first reported results from the phase 2 LINKER-SMM1 trial.

The study was presented by Paula Rodr.guez-Otero, MD, PhD, during an oral abstract session at the IMS Annual Meeting.

Dr. Rodríguez-Otero reported that linvoseltamab showed a favorable safety profile in this patient group, including the following:

- **Cytokine release syndrome was reported in 42% of patients, including grade 1–2 events. There were no cases of ICANS.**
- **Infections were reported in 79% of patients, with only three (12.5%) grade 3 events (one COVID-19, one salmonella gastroenteritis, one staphylococcal bacteremia.**
- **The investigators reported no treatment discontinuations or treatment-related deaths.**

Preliminary efficacy was also positive. Among the 19 evaluable patients, ORR was 100%, with 73.7% achieving ≥VGPR. All 12 patients with available samples were MRD-negative (10^{-6} sensitivity), and responses deepened over time, she reported.

"These early data suggest that by intervening in high-risk smoldering myeloma, when the immune system is more intact, we may significantly delay or even prevent progression to active disease," Dr. Rodríguez-Otero said.

Funding for the study was provided by Regeneron.

REFERENCE

Rodriguez-Otero P. Safety and efficacy of linvoseltamab (LINVO) in patients (Pts) with High-risk smoldering multiple myeloma (HR-SMM): first results from the phase 2 LINKER-SMM1 trial. Abstract OA-68. Presented at the 2025 International Myeloma Society Annual Meeting; September 17-20; Toronto, Canada.

INSIDER STORY

Free patient resource aims to guide those with difficult diagnoses

By: **Leah Sherwood**

Bev Lewyn was 48 years old when her life was upended by two blows in quick succession. In 2015 she was diagnosed with thyroid cancer, and only a few months later she learned she had breast cancer.

Years later, routine bloodwork showed a persistent drop in her white blood cell count, which would eventually lead to a third and more complex diagnosis: acute lymphoblastic leukemia (ALL). At the time, however, her oncologist and pathologist in Atlanta, Georgia, where Lewyn lives, failed to recognize the ALL. Downplaying the warning signs, her doctor discouraged a bone marrow biopsy, calling it "too traumatic."

Drawing on her investigative instincts from her years as a CNN research executive, Lewyn searched for the nation's top leukemia experts, ultimately emailing Hagop Kantarjian, MD, at the University of Texas MD Anderson Cancer Center.

After the initial email, Dr. Kantarjian and Lewyn spoke on the phone, and he asked her a series of questions, including whether she had recently taken steroids. When she mentioned she had taken steroids along with antibiotics for an ear infection, he said, "that's it," and explained how steroids can mask the presence of ALL.

"I emailed Dr. Kantarjian on a Friday morning," Lewyn recalled. "By Monday at 8 am, I was at MD Anderson in Houston having a bone marrow biopsy."

Her experience led her to create The Bev Strategy (thebevstrategy.com), a website for patients with cancer who need guidance as they navigate a difficult diagnosis. She said it offers unique help for people who have not yet started treatment and are experiencing what she calls the amygdala hijack phase, or shock phase.

"I looked online and found almost nothing focused on that moment," she said. "I'm trying to take you from that amygdala hijack, when you've just received the diagnosis and can't think clearly, to the point where you can begin making treatment decisions."

Lewyn launched thebevstrategy.com in 2023 just in time for that year's ASCO Annual Meeting. She said it was the perfect time to make the website live as Dr. Kantarjian was receiving the Karnofsky Award, ASCO's highest honor.

"I was like, OK, let's go ahead and do it," she said.

The Bev Strategy

Lewyn said thebevstrategy.com is a public service, free of charge, and has been reviewed by clinicians, including Dr. Kantarjian. It offers a simple mantra for patients:

"Calm your panic. Control what you can. Give yourself the tools you need right now to think straight and make good decisions."

At the heart of the Bev Strategy are five practical steps for anyone facing a life-changing diagnosis:

1. Take thorough notes to capture every detail.
2. Create a physical binder to organize test results and doctor instructions.
3. Find the best specialists, even if travel is required.
4. Make informed treatment decisions.
5. Stay positive, or as she puts it on her website, "ride the treatment ride with serenity and joy."

Taking notes and creating questions calmed her and helped her make more informed treatment decisions, she explained.

"The act of making a binder and writing everything down is a way of doing something physical to help yourself, because you will not remember everything," Lewyn said. "When I first got my breast cancer diagnosis and went back to Mayo Clinic, they told me not to expect to remember anything from the first visit because nobody does."

Lewyn also stressed that serious diagnoses require expert guidance.

"The other very important piece is that you've got to get to the right specialist," she said. "A lot of people—even very smart people—say, 'Oh, my doctor's so nice,' and that's great. But when you have something like cancer, you really need a specialist on your team, even if you just consult with them and then have your treatment done where you live."

Lewyn speaks with warmth and deep gratitude, despite the intensity of her treatments. She often says she feels lucky to have found doctors who listened and acted quickly, and she wanted to help other patients feel that same clarity and strength.

"I feel grateful every day for the doctors and friends who guided me," she said. "If my experience can help someone else think clearly in a frightening moment, then everything I went through has even greater meaning."

Lewyn added that formulating and implementing a strategy helped her keep a positive attitude because it gave her the tools to make great decisions on physicians and treatments. "Those decisions allowed me to feel lucky and know I was taking this on in the best way possible," she said.

Feeling lucky, combined with her understanding that treatment is a "ride" (with twists, turns, and sudden drops) is what allowed her to have genuine joy and serenity, she said.

Giving back

During the COVID-19 pandemic, Lewyn was receiving treatment for ALL at MD Anderson when she discovered she was having trouble getting the blood donations she needed.

"I'm O negative, and I was being denied—I needed it, but I couldn't get it," she said.

She soon learned that MD Anderson, like many hospitals at the time, faced a severe blood shortage.

"OK, we're going to work on this," she decided.

Lewyn tapped her media connections to launch a citywide blood-donation campaign, even appearing on Fox News to spread the word.

"I went back to some of my CNN colleagues, they put the word out, and then I wound up going on Fox News to publicize it—and soon after MD Anderson began receiving the donations they needed."

Her efforts brought billboards across Houston and helped replenish the blood supply for cancer patients.

Stay positive

Returning to the theme of positivity, Lewyn explained that staying connected to others and finding beauty in the everyday can help patients through their diagnoses and treatments.

"During that first intensive month, whenever I felt well enough, I'd wander the halls, and one day I went a different way and found this beautiful piece of artwork I'd never noticed—I felt so lucky to see it," she said. "Little discoveries like that really add up. I also made a point of bonding with the nurses—asking where they're from, what food their mom always made—because they're fascinating people. The more you fill those parts of yourself, the easier it becomes to stay positive, even when you're sick and exhausted."

> *If my experience can help someone else think clearly in a frightening moment, then everything I went through has even greater meaning."*

For more news, visit sohoinsider.com.

REGULATORY ROUNDUP

Tracking regulatory news worldwide

US FDA grants breakthrough therapy designation to sonrotoclax in relapsed or refractory MCL

The US Food and Drug Administration (FDA) has granted breakthrough therapy designation to sonrotoclax, a next-generation investigational BCL-2 inhibitor, in adult patients with relapsed or refractory mantle cell lymphoma (MCL). The therapy is manufactured by BeOne.

The FDA also accepted BeOne's request to join Project Orbis, a program initiated by the FDA Oncology Center of Excellence for concurrent oncology reviews among global regulators.

The FDA designation was granted based on positive topline results in the phase 1/2 BGB-11417-201 study (NCT05471843), which evaluated sonrotoclax in patients with relapsed or refractory MCL after a Bruton's tyrosine kinase inhibitor and anti-CD20 therapy.

BeOne plans to present full data at an upcoming medical meeting; the company also announced that the phase 3 confirmatory CELESTIAL-RRMCL study (BGB-11417-302; NCT06742996) is underway.

"Breakthrough therapy designation is reserved for medicines with the potential to transform outcomes for patients with serious diseases. This recognition affirms the strength of the emerging data for sonrotoclax and its potential to become a new standard of care for people with relapsed or refractory mantle cell lymphoma," said Julie Lepin, senior vice president and chief regulatory affairs officer at BeOne, in the company press release announcing the regulatory update.

FDA accepts BLA for Orca-T in hematological malignancies

The FDA has accepted the Biologics License Application (BLA) seeking approval for Orca-T, an investigational allogeneic T-cell immunotherapy for patients with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) and myelodysplastic syndromes (MDS).

The therapy was developed by OrcaBio; the Prescription Drug User Fee Act (PDUFA) target action date is April 6, 2026.

The BLA is supported by results from the phase 3 Precision-T study (NCT04013685), which evaluated Orca-T versus conventional allogeneic hematopoietic stem cell transplant in patients with AML, ALL, and MDS at high risk for poor outcomes. The study met its primary endpoint, according to the press release from the company.

"A stem cell transplant has been the only potentially curative option for many people with AML, ALL or MDS, however treatment-related toxicities too often hinder patient recovery. Acceptance of the Orca-T BLA marks a pivotal moment in our ability to deliver a first-in-class therapy designed to improve survival free from complications like [GVHD]," Nate Fernhoff, PhD, co-founder and CEO at Orca Bio, said in a company release.

In an oral abstract presented at the 51st Annual Meeting of the EBMT, investigators reported that Orca-T led to better outcomes than standard treatment for patients with blood cancers receiving myeloablative transplants from matched donors by reducing chronic graft-versus-host disease (GVHD) and improving survival compared to conventional allograft with tacrolimus/methotrexate.

The study's investigators wrote that the "results suggest Orca-T may be considered as a new standard of care for patients with hematologic malignancies and HLA-matched donors following myeloablative conditioning."

FDA authorizes new companion diagnostic for KMTA-rearranged acute leukemia

The FDA has granted a De Novo Classification Request for the CytoCell KMT2A Breakapart FISH Probe Kit PDx, a new companion diagnostic to the menin inhibitor revumenib (Revuforj®).

The diagnostic test detects clinically relevant rearrangements that occur in patients with acute leukemia. The test is accessible and has fast turnaround times, according to the test's manufacturer, OGT, a Sysmex Group company.

"Accurately identifying acute leukemia patients with KMT2Ar is a key factor in selecting appropriate therapeutic options for a group of patients who have traditionally had a very poor prognosis," Adrian Smith, CEO of OGT, said in a press release. "We are optimistic that the authorization of OGT's CDx will help this underserved patient group benefit from developments in precision oncology."

B-, T-cell lymphoma diagnostic test launched at SOHO 2025

The commercial launch of the Aventa Lymphoma test for patients with B- and T-cell lymphomas took place during the Thirteenth Annual Meeting of the Society of Hematologic Oncology.

The test will help guide clinicians to a clearer diagnosis, according to the test's manufacturer, Arima Genomics.

"Our goal is to reduce blind spots in lymphoma diagnosis by offering an ultrasensitive test that uncovers the full spectrum of clinically meaningful rearrangements—whether or not they are initially considered," said Chris Roberts, chief product officer for Arima Genomics and executive director for the Aventa clinical testing service, in a press release by the company.

The Aventa Lymphoma test analyzes 417 genes in a single whole-genome assay, detecting gene fusions and rearrangements missed by traditional fluorescence in situ hybridization (FISH). It conserves tissue and clarifies ambiguous diagnoses for better lymphoma classification and treatment planning, according to Arima Genomics.

The test is offered through Arima's CLIA-certified laboratory, and the test received Proprietary Laboratory Analysis code 0592U from the American Medical Association.

"The Aventa Lymphoma test can uncover gene fusions and rearrangements that may be missed by traditional FISH testing, ensuring clinically significant abnormalities are not overlooked. This transformative tool enhances patient care," said Ying Zou, MD, PhD, the director of the Cancer Cytogenetic Laboratory, Cytogenomic Research Core and associate director of the Molecular Diagnostics Laboratory at Johns Hopkins University. "In lymphomas exhibiting atypical FISH signal patterns across multiple biomarkers, the Aventa Lymphoma test identified actionable genetic alterations, significantly enhancing diagnostic precision, subtype classification, prognostic evaluation, and tailored treatment strategies."

FDA approves revumenib in relapsed or refractory NMP1-mutated AML

The FDA has approved revumenib (Revuforj®) in patients with relapsed or refractory NPM1-mutated AML. The approval is indicated for both adult and pediatric patients one year and older who have no alternative treatment options.

The therapy has another indication for the treatment of relapsed or refractory acute leukemia with a KMT2A translocation in adult and pediatric patients one year and older. That indication was approved by the FDA in 2024.

Syndax Pharmaceuticals, the manufacturer of revumenib, said that the second indication is the only menin inhibitor FDA-approved for multiple AML subtypes.

"We are thrilled to have secured a second indication for Revuforj, making it the first and only menin inhibitor that is FDA-approved for multiple acute leukemia subtypes in both adults and children. The breadth of the indicated patient population highlights the compelling and consistent efficacy and tolerability of Revuforj in multiple different types of patients," said Michael A. Metzger, CEO. "Our launch into this second population will greatly benefit from physicians' already strong familiarity with Revuforj and positive experience treating well over 1,000 patients in clinical trials and nearly one year of commercial use."

According to the company release, the safety evaluation of revumenib was based on the FDA's analysis of 241 patients (207 adult and 34 pediatric patients) with relapsed or refractory NPM1-mutated or KTM2A-translocated acute leukemia who were treated with revumenib in clinical trials.

FDA approves blenrep combo in relapsed or refractory MM

The FDA has approved belantamab mafodotin (blenrep) in combination with bortezomib and dexamethasone (BVd) for the treatment of adult patients with relapsed or refractory multiple myeloma (MM) who have received at least two prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory (IMID) agent.

The approval is based on the DREAMM-7 study, a phase 3, open-label, randomized, controlled trial, which previously demonstrated a significant progression-free survival benefit with blenrep compared with daratumumab, bortezomib, and dexamethasone.

In patients who had two or more prior lines of therapy, including a PI and an IMID, blenrep in combination demonstrated a clinically meaningful 51% reduction in the risk of death (HR 0.49; 95% CI, 0.32-0.76) and a tripled median progression-free survival (PFS) of 31.3 months (95% CI, 23.5-NR) versus 10.4 months (95% CI, 7.0-13.4) for a daratumumab-based triplet (HR 0.31, 95% CI, 0.21-0.47). The safety and tolerability profiles of the blenrep combination were broadly consistent with the known profiles of the individual agents, according to GSK, the manufacturer of the therapy.

"With the approval of blenrep, we now have a community-accessible BCMA-targeting agent with the potential to improve outcomes for patients following two or more prior lines of treatment, where options are limited," Sagar Lonial, MD, FACP, said in a press release from GSK. "This approval marks an important advance in the US relapsed/refractory treatment landscape."

FDA grants orphan drug designation to MDS investigational therapy ofirnoflast

The FDA has granted orphan drug designation to ofirnoflast (HT-6184), an investigational therapy for myelodysplastic syndromes (MDS).

Ofirnoflast, a NEK7 inhibitor, is manufactured by clinical-stage biopharmaceutical company Halia Therapeutics. The therapy completed a phase 2 study evaluating safety and outcomes in MDS.

"This designation underscores the potential of our approach in myelodysplastic syndromes and supports our commitment to developing new treatment options for patients living with MDS," said David Bearss, PhD, CEO of Halia Therapeutics, in a company release announcing the designation. "Ofirnoflast represents a first-in-class approach to modulating inflammasome biology, an upstream driver of inflammation, with the goal of restoring healthy bone marrow function."

IN MEMORIAM

World-renowned hematologist Brian G.M. Durie, MD, dead at the age of 82

World-renowned hematologist Brian G.M. Durie, MD, has died at the age of 82. Dr. Durie's death was announced on October 14, 2025, in a press release by the International Myeloma Foundation (IMF), which Dr. Durie co-founded in 1990.

"Dr. Durie was a giant in the field like no other. He leaves behind a legacy that will endure forever—from his incredible contributions to myeloma research to the superb care and counseling he provided patients; from educating almost all practicing myeloma experts today to helping advance patient care through important clinical trials; from developing the Durie-Salmon Staging System to co-founding the IMF, a patient-centered organization, which he led for three decades. He had an enormous impact—not just on myeloma but on all of oncology. I have lost a dear friend and mentor and will forever cherish his kindness," said IMF Chairperson of the Board S. Vincent Rajkumar, MD.

Dr. Durie was born in December 1942 in Gullane, Scotland. He graduated from the University of Edinburgh Medical School in 1966 and moved to the United States to complete his medical residency and subspecialty training at the Mayo Clinic in Minnesota. In 1989, he became a professor and Head of the Department of Clinical and Laboratory Hematology at the University of London, where he also established a myeloma program. In 1992, he returned to the United States in the Division of Hematology/Oncology at Cedars-Sinai Medical Center in Los Angeles, where he served as a myeloma specialist physician, according to the IMF.

Dr. Durie is survived by his wife, Susie Durie, his daughter, Annabel Reardon, and his son, Benjamin Durie, along with his four grandchildren. Those wishing contact the family may contact Annabel Reardon at annabelreardon@outlook.com.

GLOBAL SOHO

SOHO KSA holds 1st meeting in the region

SOHO KSA held its first regional meeting in Riyadh, the Kingdom of Saudi Arabia (KSA). The two-day event was held at the Intercontinental Hotel on October 25 –27 and was Organized by King Faisal Specialist Hospital & Research Centre. All photos courtesy of SOHO Ambassador Dr. Chokri Ben Lamine.

SOHO MENA returns to in-person meeting for the region's 3rd meeting

SOHO MENA took place on September 25–27 in Beirut, Lebanon, and marked a return to in-person collaboration after the meeting was held in a virtual format in 2024 due to the war in the region.

Now in its third year, the meeting featured a comprehensive program covering all blood cancers, bringing together world-class clinicians including Drs. Hagop Kantarjian, Courtney DiNardo, Elias Jabbour, Naval Daver, Rami Komrokji, and Amer Zeidan for lively discussions and exchange of ideas.

MARK YOUR CALENDARS!

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Fourteenth Annual Meeting of the Society of Hematologic Oncology

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