FOR PATIENTS, SURVIVORS & THEIR CAREGIVERS

HEMATOLOGY

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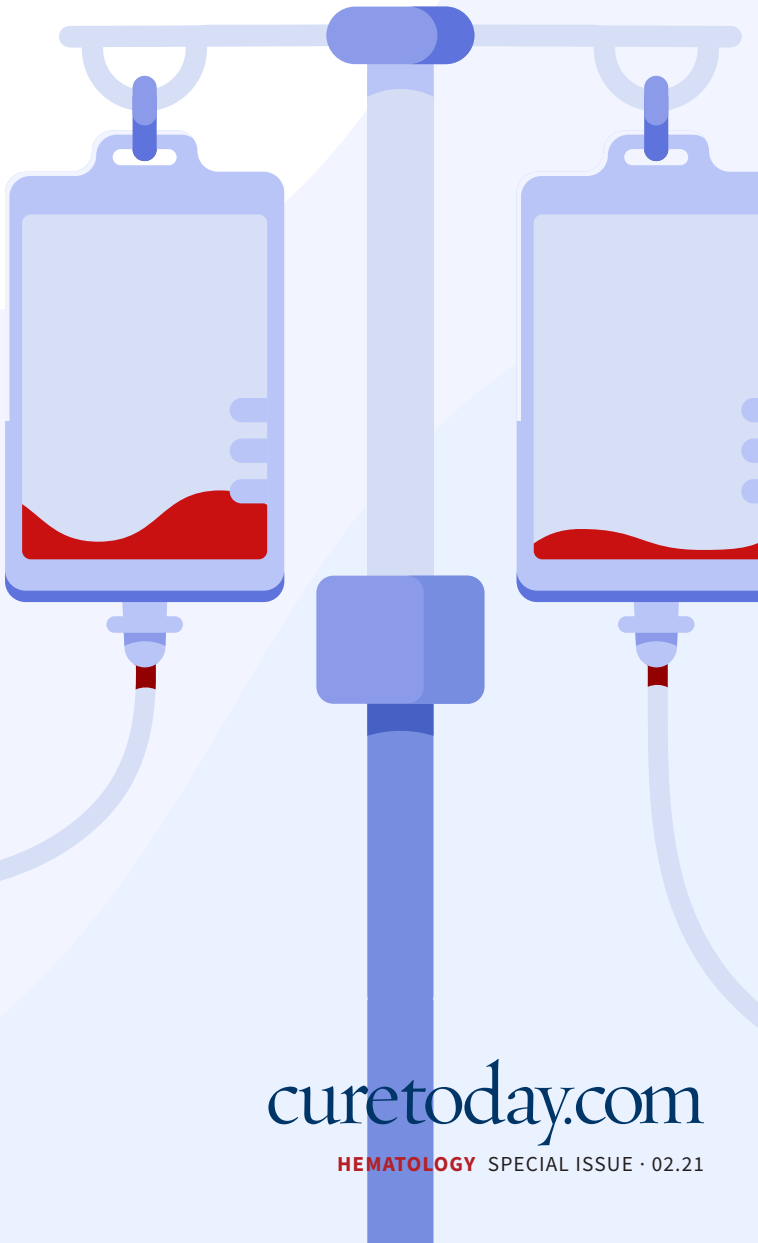
Cancer Updates, Research & Education®

KEEP IT Flowing

Combating COVID-19 Blood Shortages

Collaborating to ensure there's enough blood for transfusions in hematologic malignancies



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Predicting worse survival benefits

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HEMATOLOGIC MALIGNANCIES
Further mental health screening is needed for those recently diagnosed with a blood cancer

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HEMATOLOGY SPECIAL ISSUE · 02.21

IMPORTANT SAFETY INFORMATION

What is XPOVIO?

XPOVIO® (selinexor) is a prescription medicine used:

- in combination with bortezomib and dexamethasone to treat adult patients with multiple myeloma who have received at least one prior therapy.

It is not known if XPOVIO is safe and effective in children less than 18 years of age.

Your healthcare provider will do blood tests before you start taking XPOVIO, and often during the first 3 months of treatment, and then as needed during treatment.

XPOVIO can cause serious side effects, including:

- **Low platelet counts.** Low platelet counts are common with XPOVIO and can lead to bleeding, which can be severe and can sometimes cause death. Your healthcare provider may prescribe platelet transfusions or other treatments for your low platelet counts. **Tell your healthcare provider right away if you have any bleeding or easy bruising during treatment with XPOVIO.**
- **Low white blood cell counts.** Low white blood cell counts are common with XPOVIO and can sometimes be severe. You may have an increased risk of getting bacterial infections during treatment with XPOVIO. If needed, your healthcare provider may prescribe antibiotics if you have signs or symptoms of infection.
- **Serious infections.** Infections are common with XPOVIO and can be serious and can sometimes cause death. This includes upper or lower respiratory tract infections, such as pneumonia, and an infection throughout your body (sepsis). **Tell your healthcare provider right away if you have any signs or symptoms of an infection such as cough, chills, or fever during treatment with XPOVIO.**
- **Neurologic side effects.** XPOVIO can cause dizziness, fainting, decreased alertness, and changes in your mental status, including problems with thinking, seeing or hearing things that are not really there (hallucinations). These problems can sometimes be severe and life-threatening. **Tell your healthcare provider right away if you get any of these symptoms. Do not drive or operate heavy or dangerous machinery until you know how XPOVIO affects you. Take precautions to prevent a fall.**
- **Nausea, vomiting and/or diarrhea.** Nausea, vomiting and/or diarrhea can occur when you take XPOVIO and can sometimes be severe. You may be at risk for becoming dehydrated. Your healthcare provider may prescribe anti-nausea or anti-diarrhea medicines.
- **Loss of appetite and weight loss.** Loss of appetite and weight loss are common with XPOVIO. Tell your healthcare provider if you have a decrease or loss of appetite and if you are losing weight.
- **Decreased sodium levels in your blood.** Decreased sodium levels in your blood are common with XPOVIO. Your healthcare provider may talk with you about your diet and prescribe IV fluids or salt tablets.
- **New or worsening cataract, cloudiness, or loss of transparency of the lens in the eye.** New or worsening cataract are common with XPOVIO. If a cataract forms, your vision may decrease, and you may need eye surgery to remove the cataract and restore your vision. **Tell your healthcare provider right away if you have symptoms of a cataract such as double vision, blurred vision, or sensitivity to light or glare.**

Common side effects of XPOVIO include:

- tiredness
- weakness
- low red blood cell count (anemia). Symptoms may include tiredness and shortness of breath
- constipation
- shortness of breath
- increased blood sugar
- changes in body salt and mineral levels in your blood
- changes in kidney and liver function blood tests

These are not all of the possible side effects of XPOVIO.

Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

Before taking XPOVIO, tell your healthcare provider about all of your medical conditions, including if you:

- have or have had a recent or active infection
- have or have had bleeding problems
- are pregnant or plan to become pregnant. XPOVIO can harm your unborn baby
- are taking prescription and over-the-counter medicines, vitamins, and herbal supplements

Ability to have children: XPOVIO may affect the ability of both women and men to have children. Talk to your healthcare provider if you have concerns about fertility.

Females who are able to become pregnant: Your healthcare provider will check to see if you are pregnant before you start taking XPOVIO. You should use effective birth control (contraception) during treatment with XPOVIO and for 1 week after your last dose, as XPOVIO can harm an unborn baby. Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with XPOVIO. Do not breastfeed during treatment with XPOVIO and for 1 week after your last dose of XPOVIO. It is not known if XPOVIO passes into your breast milk.

Males with female partners who are able to become pregnant should use effective birth control during treatment with XPOVIO and for 1 week after your last dose.

Please see the Medication Guide and the full Prescribing Information for XPOVIO.

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Karyopharm® Therapeutics

XPOVIO®
(selinexor)

NEW INDICATION
FOR PATIENTS WITH MULTIPLE MYELOMA

Your doctor may prescribe XPOVIO, the only FDA-approved medication of its kind, as early as 1st relapse in multiple myeloma.

XPOVIO® (selinexor) is **now approved** in combination with other treatments (bortezomib and dexamethasone) to treat adult patients with multiple myeloma who have received at least one prior therapy.

LEARN MORE ABOUT TREATMENT AT XPOVIO.COM

PATIENT INFORMATION

XPOVIO® (x-PO-Vee-O)
(selinexor)
Tablets

XPOVIO® (selinexor)

What is XPOVIO?

XPOVIO is a prescription medicine used in combination with the medicines VELCADE® (bortezomib) and dexamethasone to treat adults with multiple myeloma (MM) who have received at least one prior treatment for their disease.

It is not known if XPOVIO is safe and effective in children less than 18 years of age.

What is the most important information I should know about XPOVIO?

XPOVIO can cause serious side effects, including:

- **Low platelet counts.** Low platelet counts are common with XPOVIO and can lead to bleeding which can be severe and can sometimes cause death. Your healthcare provider may prescribe platelet transfusions or other treatments for your low platelet counts.
  Tell your healthcare provider right away if you have any bleeding or easy bruising during treatment with XPOVIO.
- **Low white blood cell counts.** Low white blood cell counts are common with XPOVIO and can sometimes be severe. You may have an increased risk of getting bacterial infections during treatment with XPOVIO. Your healthcare provider may prescribe antibiotics if you have signs or symptoms of infection, or certain medicines to help increase your white blood cell count, if needed.

Your healthcare provider will do blood tests before you start taking XPOVIO, and often during the first 3 months of treatment, and then as needed during treatment to monitor you for side effects.

Your healthcare provider may change your dose of XPOVIO, stop your treatment for a period of time, or completely stop your treatment if you have certain side effects during treatment with XPOVIO.

See "What are the possible side effects of XPOVIO?" for more information about side effects.

What should I tell my healthcare provider before taking XPOVIO?

Before taking XPOVIO, tell your healthcare provider about all of your medical conditions, including if you:

- have or have had a recent or active infection.
- have or have had bleeding problems.
- are pregnant or plan to become pregnant. XPOVIO can harm your unborn baby.
  Females who are able to become pregnant:
  - Your healthcare provider will check to see if you are pregnant before you start taking XPOVIO.
  - You should use effective birth control (contraception) during treatment with XPOVIO and for 1 week after your last dose.
  - Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with XPOVIO.

  Males with female partners who are able to become pregnant:
  - You should use effective birth control during treatment with XPOVIO and for 1 week after your last dose.
- are breastfeeding or plan to breastfeed. It is not known if XPOVIO passes into your breast milk.
  - Do not breastfeed during treatment with XPOVIO and for 1 week after your last dose of XPOVIO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Talk with your healthcare provider before taking any new medicines.

How should I take XPOVIO?

- Take XPOVIO exactly as prescribed by your healthcare provider.
- Your healthcare provider will prescribe dexamethasone with your XPOVIO treatment. Take dexamethasone exactly as prescribed.
- Your healthcare provider will tell you how much XPOVIO to take and when to take it. Do not change your dose or stop taking XPOVIO without talking to your healthcare provider first.
- Swallow XPOVIO tablets whole with water. **Do not break, chew, crush, or divide the tablets.**
- Be sure to take any medicines prescribed by your healthcare provider before and during treatment with XPOVIO to help prevent nausea and vomiting. Tell your healthcare provider if the prescribed medicine does not control your nausea and vomiting.
- It is important for you to drink enough fluids to help prevent dehydration and to eat enough calories to help prevent weight loss during treatment with XPOVIO. Talk to your healthcare provider if this is a problem for you. **See "What are the possible side effects of XPOVIO?"**
- If you miss a dose of XPOVIO, take your next dose at your next regularly scheduled day and time.
- If you vomit after taking a dose of XPOVIO, do not take an extra dose. Take your next dose at your next regularly scheduled day and time.
- If you take too much XPOVIO, call your healthcare provider right away.

What should I avoid while taking XPOVIO?

XPOVIO can cause neurologic side effects.

- **See "What are the possible side effects of XPOVIO?" below.**
- If you have any neurologic side effects with XPOVIO, **do not drive or operate heavy or dangerous machinery until your neurologic side effects go away.**
- **Avoid falling.** Use care as needed to avoid falling due to neurologic side effects.

What are the possible side effects of XPOVIO?

XPOVIO can cause serious side effects, including:

- **See "What is the most important information I should know about XPOVIO?"**
- **Nausea and vomiting.** Nausea and vomiting are common with XPOVIO and can sometimes be severe. Nausea and vomiting may affect your ability to eat and drink well. You can lose too much body fluid and body salts (electrolytes) and may be at risk for becoming dehydrated. You may need to receive intravenous (IV) fluids or other treatments to

help prevent dehydration. Your healthcare provider will prescribe anti-nausea medicines for you to take before you start and during treatment with XPOVIO. **See "How should I take XPOVIO?"**

- **Diarrhea.** Diarrhea is common with XPOVIO and can sometimes be severe. You can lose too much body fluid and body salts (electrolytes) and may be at risk for becoming dehydrated. You may need to receive IV fluids or other treatments to help prevent dehydration. Your healthcare provider will prescribe anti-diarrhea medicine for you as needed.
- **Loss of appetite and weight loss.** Loss of appetite and weight loss are common with XPOVIO and can sometimes be severe. Tell your healthcare provider if you have a decrease or loss of appetite and if you notice that you are losing weight at any time during treatment. Your healthcare provider may prescribe medicines that can help increase your appetite or prescribe other kinds of nutritional support. Your healthcare provider will monitor your appetite and weight before you start XPOVIO and often during the first 3 months, then as needed during treatment.
- **Decreased sodium levels in your blood.** Decreased sodium levels in your blood is common with XPOVIO but can also sometimes be severe. Low sodium levels in your blood can happen if you have nausea, vomiting, or diarrhea, you become dehydrated, or if you have loss of appetite with XPOVIO. You may not have any symptoms of a low sodium level. Your healthcare provider may talk with you about your diet and prescribe IV fluids for you based on the sodium levels in your blood. Your healthcare provider will do blood tests before you start taking XPOVIO, and often during the first 2 months of treatment, and then as needed during treatment to monitor the sodium levels in your blood.
- **Serious infections.** Infections are common with XPOVIO and can be serious and can sometimes cause death. XPOVIO can cause infections including upper or lower respiratory tract infections, such as pneumonia, and an infection throughout your body (sepsis). **Tell your healthcare provider right away if you have any signs or symptoms of an infection such as cough, chills or fever, during treatment with XPOVIO.**
- **Neurologic side effects.** XPOVIO can cause neurologic side effects that can sometimes be severe and life-threatening.
  - XPOVIO can cause dizziness, fainting, decreased alertness, and changes in your mental status including confusion and decreased awareness of things around you (delirium).
  - In some people, XPOVIO may also cause problems with thinking (cognitive problems), seeing or hearing things that are not really there (hallucinations), and they may become very sleepy or drowsy.
  - Taking other medicines that can cause dizziness or mental status changes during treatment with XPOVIO may increase your risk of neurologic side effects.

Tell your healthcare provider right away if you get any of these signs or symptoms.

- **New or worsening cataract, a cloudy or loss of transparency of the lens in the eye.** New or worsening cataract are common with XPOVIO. If a cataract forms, your vision may decrease, and you may need eye surgery to remove the cataract and restore your vision. **Tell your healthcare provider right away if you have symptoms of a cataract such as double vision, blurred vision, sensitivity to light or glare.**

Your healthcare provider may change your dose of XPOVIO, stop your treatment for a period of time, or completely stop your treatment if you have certain side effects during treatment with XPOVIO.

Common side effects of XPOVIO include:

- tiredness
- low red blood cell count (anemia). Symptoms may include tiredness and shortness of breath.
- increased blood sugar
- changes in body salt and mineral levels in your blood
- changes in kidney and liver function blood tests

XPOVIO may cause fertility problems in males and females, which may affect your ability to have children. Talk to your healthcare provider if you have concerns about fertility.
These are not all the possible side effects of XPOVIO.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store XPOVIO?

- Store XPOVIO at or below 86°F (30°C).
- XPOVIO comes in a child-resistant blister pack.

Keep XPOVIO and all medicines out of the reach of children.

General information about the safe and effective use of XPOVIO.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use XPOVIO for a condition for which it was not prescribed. Do not give XPOVIO to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about XPOVIO that is written for health professionals.

What are the ingredients in XPOVIO?
Active ingredient: selinexor
Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, Opadry 200 clear, Opadry II blue, povidone K30, and sodium lauryl sulfate.
Manufactured for and marketed by: Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, MA, 02459
XPOVIO is a registered trademark of Karyopharm Therapeutics Inc. All other trademarks are the property of their respective owners.

For more information, call 1-888-209-9326 or go to www.XPOVIO.com.
Based on Medication Guide approved by the U.S. Food and Drug Administration, as revised in December 2020.

Karyopharm® Therapeutics

US-XPOV-01/21-00021 (01/21)

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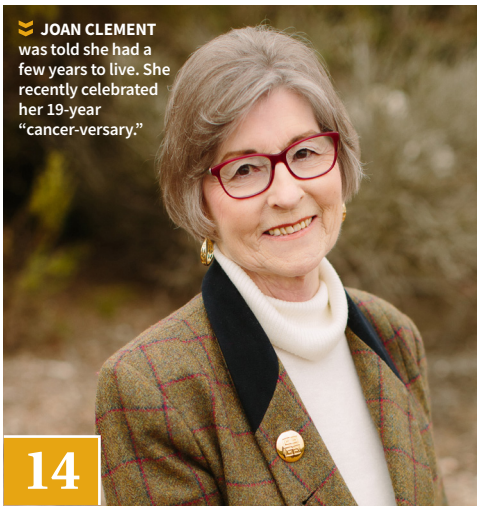

JOAN CLEMENT was told she had a few years to live. She recently celebrated her 19-year "cancer-versary."

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MARIE FUESEL received blood products more than 100 times during treatment.

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KEITH OWENS went to the hospital for bloodwork and left one month later.

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Team Efforts Propel Cancer Victories

TRYING TO GET THROUGH ANYTHING in life alone, especially a cancer diagnosis, can be a daunting challenge. It's always best to have a team of people, whether friends or family, rooting us on as we face whatever challenges come our way.

But sometimes, we lose sight of the significance of teamwork. I was reminded of that recently when former NFL player Devon Still addressed the virtual audience at CURE Media Group's eighth annual MPN Heroes® program in December.

> "It's always best to have a team ... rooting us on as we face whatever challenges come our way."

Still stressed that teamwork — in this instance, overcoming a blood cancer diagnosis — is pivotal to reaching the goal of victory.

Within these pages, you will meet people who embraced that team mentality and continued to persevere to help themselves and others in the myeloproliferative neoplasm (MPN) community.

Also within this special issue, a feature story explores one of the many disastrous effects of the COVID-19 pandemic and what cancer centers, hospitals and even cancer survivors have done to mitigate that issue.

The problem, as oncologists attest, is that as the pandemic spread, many avid blood donors canceled their scheduled appointments. What has concerned hematology/oncology experts is that, according to the American Red Cross, patients with cancer use nearly one-quarter of the U.S. blood supply, and donated blood is often used during the treatment of patients with hematologic malignancies to control bleeding.

As a result of these shortages, several cancer centers have adjusted their policies and thresholds for transfusing blood. Of note, one leukemia survivor featured in the story spent the first few months of the pandemic organizing five small blood drives in a Chicago suburb. Because of those successes, she was asked to help run the seventh annual ABC 7 Great Chicago Blood Drive, which collected more than 2,000 units of blood.

Also inside: how advancements in CAR-T cell therapy have begun to revolutionize the treatment of T-cell leukemias, as well as a recap of some of the groundbreaking advancements in the treatment of blood cancers that were presented at a recent major medical meeting.

As always, thank you for reading. C

MIKE HENNESSY SR.
Chairman and Founder

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is proud to be partners with a number of leading advocacy groups across the country, giving them national reach and visibility for their cutting edge initiatives, programs, content, research and thought leadership.

Treatment Advances Transform CML Into Chronic Disease

MIKE KITADA

OVER THE PAST DECADE, advances in both diagnostics and therapeutics in a variety of blood cancers have turned certain diseases into chronic conditions. In particular, chronic myeloid leukemia (CML) has become a disease that used to almost always progress within months to years after diagnosis, but CML now is almost cured thanks to the number of inhibitors made available for treatment and very structured follow-up algorithms and tests.

CML makes up about 15% of leukemias, with the majority of cases occurring in adults. While the number of people diagnosed with CML increased by 2% annually from 2007 to 2016, deaths from the disease decreased by about 1% each year from 2008 to 2017.

This can be attributed, in large part, to recent scientific advances in targeted treatments, all of which were enabled by elegant laboratory studies that identified a genetic mutation that drives this disease. The result of this mutation (a result of a fusion of two genes) creates a growth-driving enzyme known as the BCR-ABL kinase that can be targeted with synthetic molecules that block its activity.

For most with CML, treatment doesn't end, as patients stay on a tyrosine kinase inhibitor (TKI) indefinitely to keep their disease in check. Currently approved by the Food and Drug Administration, TKIs for the treatment of CML include Gleevec (imatinib) — which was the first to be approved in this disease space in 2001 — as well as Bosulif (bosutinib), Sprycel (dasatinib), Tasigna (nilotinib) and Iclusig (ponatinib). Blood analyses that can detect tiny amounts of RNA made from the BCR-ABL fusion gene allow for very early detection of resistance to therapy and the need to change to another drug.

Following the addition of these TKIs to the treatment armamentarium, the five-year survival rate for patients diagnosed with CML has more than tripled since the mid-1970s.

With such advances, we've allowed patients to return to the life they had before cancer, but it is also key to emphasize that patients will be monitored for the rest of their lives.

Next, the key question has become: Can I safely stop treatment? We are seeing more and more that for some, this is possible, while others have the option to lower the dose they are taking to minimize side effects.

DEBU TRIPATHY, M.D.
Editor-in-Chief
Professor of Medicine
Chair, Department of Breast Medical Oncology
The University of Texas MD Anderson Cancer Center

News & Insights From the Virtual 2020 American Society of Hematology Annual Meeting & Exposition, Held Dec. 5-8

COMPILED *by* KRISTIE L. KAHL

Mental Health Screening and Management Is Needed for Patients With Blood Cancers

MORE THAN 1 IN 5 people experienced depression or anxiety before or not long after receiving a blood cancer diagnosis, highlighting the need for further mental health screening in these individuals, according to data from a recent analysis.

"These mental health disorders can decrease the quality of life, delay onset of cancer therapy and even decrease overall survival," said Dr. Thomas M. Kuczmarski, a resident physician at Brigham and Women's Hospital in Boston, during a virtual presentation of the data at the meeting.

The researchers evaluated the prevalence of mental health disorders in a group of patients with blood cancers who were age 67 years and older, including those with lymphoma (53.4%), myeloma (18.6%), leukemia (18%) or myelodysplastic syndromes (10%). They measured patients' depression or anxiety prior to diagnosis, as well as cancer-associated depression or anxiety that occurred one month prior to or three months after their cancer diagnoses.

Among the entire patient population, 20.7% had at least one of the assessed mental health disorders, some of the patients (10.6%) had depression prior to their diagnosis and an additional 4.4% developed depression associated with their cancer.

Anxiety before diagnosis was seen in 7.4% of the patients, and 2.8% developed the mental health disorder after diagnosis.

"Given our finding that the biggest risk factor for developing cancer-associated depression or anxiety was actually a preexisting mental health disorder, we believe that additional psychosocial support for individuals with baseline mental health illness is crucial," said Kuczmarski.

Targeted Therapy Combination May Benefit Patients With Waldenström's Macroglobulinemia

PATIENTS WITH WALDENSTRÖM'S macroglobulinemia, a slow-growing type of non-Hodgkin lymphoma, who were treated with Imbruvica (ibrutinib) plus Rituxan (rituximab) had better response and survival outcomes nearly five years after therapy compared with those treated with placebo plus Rituxan.

Data from a phase 3 trial that included 150 patients with the disease analyzed progression-free survival (the time from treatment to disease progression), overall survival, response rates and safety.

At almost five years following treatment, rates of progression-free survival were 68% in the Imbruvica plus Rituxan group compared with 25% in the placebo plus Rituxan group. Overall survival was greater in the Imbruvica plus Rituxan group (86%) than the placebo plus Rituxan group (84%). The combination regimen also led to an increased number of patients who experienced a partial response compared with those treated with placebo (76% versus 31%). Of note, survival and response benefits were

observed regardless of genotype or prior treatment received.

The most common grade 3 to 4 side effects, or more serious events, included hypertension (high blood pressure), atrial fibrillation (irregular heart rhythm), anemia and neutropenia (a low count of neutrophils, or a type of white blood cell).

"When you add (Imbruvica), it looks like the response rates and also the (progression-free survival) largely act independently of the genotype," said Dr. Christian Buske, medical director at the Comprehensive Cancer Center Ulm at the Institute of Experimental Cancer Research at University Hospital Ulm in Germany, during the discussion after his virtual presentation. "I think this is particularly interesting for patients who carry a (mutation). … In addition, what we see is that (added side effects with the addition of Imbruvica), it looks like that the time to response, to measure response is shorter. This is an indication for treatment but also for clinicians because it's for sure an advantage when we see that this approach we are selecting for this patient indeed works and helps the patient."

Calquence Induces Limited Heart Toxicities in Patients With Chronic Lymphocytic Leukemia

TREATMENT WITH CALQUENCE (acalabrutinib) alone led to a low incidence of heart-related toxicities in patients with chronic lymphocytic leukemia (CLL), which resulted in few treatment discontinuations, according to data from an analysis of four clinical trials.

Although Bruton tyrosine kinase (BTK) inhibitors, such as Calquence and Imbruvica (ibrutinib), have demonstrated to be effective in the treatment of B-cell malignancies such as CLL, previous study results have shown an increase in cardiovascular toxicities associated with the use of Imbruvica. However, since Calquence is a more selective BTK inhibitor than Imbruvica in lab tests, the researchers hypothesized that treating patients with only Calquence may result in fewer toxicities.

At a median follow-up of more than two years, 17% of the patient population who received Calquence alone experienced a cardiac toxicity of any severity. Seven patients had to discontinue treatment because of the side effect. Notably, the data demonstrated that 91% of patients who experienced a cardiac toxicity had one or more preexisting risk factors before receiving the medication.

In total, 37 patients experienced cardiac events that were grade 3 or higher. Of those patients, 49% continued to receive Calquence at the time researchers stopped collecting data.

In addition, the median time to onset of cardiac events was 10.1 months. Of 38 patients who experienced atrial fibrillation/flutter while receiving treatment, 18% had a history of arrhythmia or atrial fibrillation/flutter. Of 67 patients who experienced hypertension events while receiving Calquence, 69% had prior hypertension and 27% had risk factors.

The most common cardiac events of any severity were atrial fibrillation (44 events), palpitations (27 events) and tachycardia, or fast heart rate, (17 events).

Addition of Daratumumab to Standard Regimen Improves Clinical Benefit in Relapsed/Refractory Myeloma

PATIENTS WITH MULTIPLE MYELOMA whose disease had relapsed or stopped responding to treatment reduced their risk of disease progression or death after receiving a three-drug combination, according to results from the APOLLO study.

The phase 3 clinical trial included 304 patients and researchers evaluated adding Darzalex (daratumumab), which is given as an injection under the skin into the tissue layer, to the standard treatment of Pomalyst (pomalidomide) and dexamethasone. Patients had to have relapsed/refractory multiple myeloma and received one or more prior types of therapy. The researchers then compared this combination with the standard regimen alone.

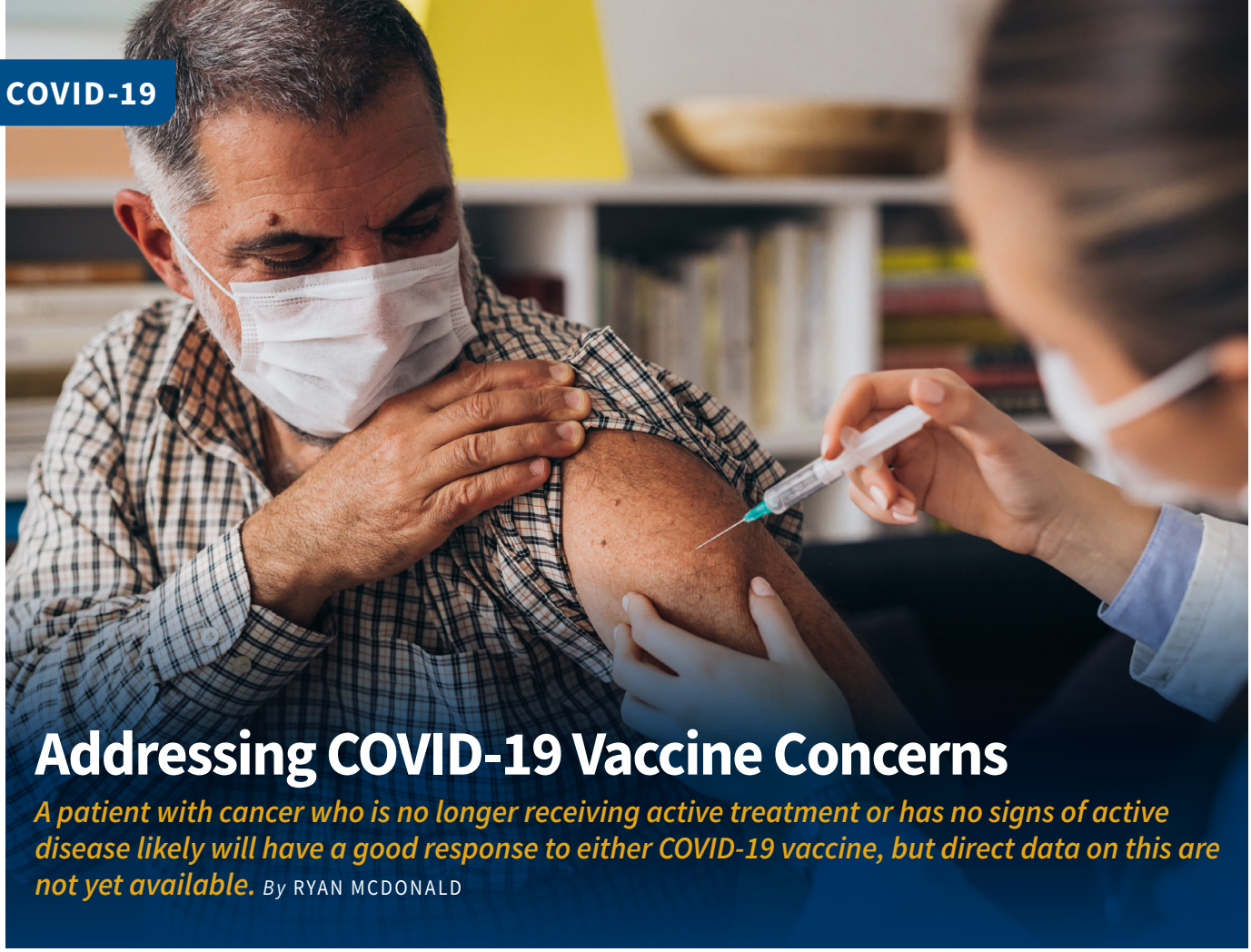
The data showed that the addition of Darzalex demonstrated better progression-free survival (the time from treatment to disease progression; 12.4 months versus 6.9 months), leading to a 37% reduction in the risk of progression or death, compared with Pomalyst and dexamethasone alone.

Moreover, the three-drug combination had a higher complete response rate (25%) versus the standard regimen (4%). Minimal residual disease (the amount of leukemia cells that remain in a person during or after treatment) negativity was 9% versus 2%, respectively.

DR. MELETIOS A. DIMOPOULOS

The most common grade 3 to 4 side effects with the addition of Darzalex compared with the standard regimen included neutropenia (a low count of neutrophils, or a type of white blood cell; 68% versus 51%), leukopenia (reduced number of white blood cells and an increased risk of infection; 17% versus 5%), lymphopenia (a condition where the blood is missing lymphocytes, or white blood cells; 12% versus 3%), febrile neutropenia (fever during a period of significant neutropenia; 9% versus 3%) and pneumonia (13% versus 7%).

"The vast increasing convenience for patients in decreasing treatment burden (shows that) we could conclude that subcutaneous D-Pd is an effective and convenient treatment for patients with relapsed/refractory multiple myeloma who have received at least one prior line of therapy, including (Revlimid [lenalidomide]) or a proteasome inhibitor," concluded Dr. Meletios A. Dimopoulos, from the National and Kapodistrian University of Athens in Greece.



Addressing COVID-19 Vaccine Concerns

A patient with cancer who is no longer receiving active treatment or has no signs of active disease likely will have a good response to either COVID-19 vaccine, but direct data on this are not yet available. By RYAN MCDONALD

FOLLOWING THE RECENT EMERGENCY use authorization of the Pfizer-BioNTech and Moderna COVID-19 vaccines by the Food and Drug Administration (FDA), many patients with cancer who are actively receiving treatment — and those who no longer have signs of active disease — may have questions about the vaccines.

Dr. Debu Tripathy, professor and chair of the Department of Breast Medical Oncology, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center, in Houston and editor-in-chief of *CURE*®, said he and his colleagues were getting questions about the distribution of the vaccines even prior to their authorization.

"All our patients want to know what the schedule is for when they might get a vaccine," Tripathy said in an interview with *CURE*®.

CURE® recently spoke with Tripathy and Dr. Roy Chemaly, chief infection control officer and a professor in the Department of Infectious Diseases, Infection Control and Employee Health, at MD Anderson, about the vaccine.

DECIDING WHO GETS THE VACCINE IS A PROCESS

In December 2020, high-risk health care workers started receiving the vaccines across the United States. Many frontline workers have received either vaccine over the past several months, including those who work directly with patients with cancer who are at a high risk for infection.

After those front-line workers, there is a process for which patients will begin to receive the vaccine, Tripathy said.

Patients with underlying conditions at high risk for complications of COVID-19 infection will likely be a top priority to receive either vaccine. However, for patients with cancer receiving therapy, particularly, those receiving more intensive therapies such as stem cell transplants, some details still need to be ironed out.

"We haven't gotten into the nitty-gritty in terms of how we're going to divide (the vaccines) to some extent," Tripathy said. "We're going to have the physicians be involved in prioritizing this based on their knowledge because they're the ones who know the patients best."

Chemaly also noted that the vaccines will likely be administered to patients on a case-by-case basis.

"For cancer patients who are still under active treatment with (chemotherapy) or radiation or early after stem cell transplantation, there are no data on how effective the (vaccines are) and (how they) should be used," he said. "So we're going to be a little bit more cautious and take it case by case to recommend these vaccines to our cancer patients, as we wait for more data to come out from the general population, then see how safe it is and how effective (it is) in order to really extrapolate to our cancer patients."

If a patient is no longer receiving active treatment and there are no signs of active cancer, Chemaly said, they

should have a good response to the vaccines, and it will likely be safe for them to receive either one.

"Now, for other patients who (are) in the follow-up period, not really called 'survivors' of cancer, we're going to probably provide some guidance; for example, for recipients of a stem cell transplantation. If it's been six months from allogeneic transplantation, they're stable and recovering well after transplant, then it is probably safe to give it to these patients," he said. "Autologous transplant could be three months from the transplantation if they have no active issues, they are still in remission, and they're stable enough to receive a vaccine."

"Nothing works unless you get the vaccine. If you don't get the vaccine, all of this was for nothing."

— DR. DEBU TRIPATHY

IT IS NOT KNOWN WHAT SIDE EFFECTS MAY OCCUR

As with any vaccine, Tripathy said, some people will have reactions, but at least there are data from healthy individuals that can be shared with patients with cancer. However, there will be some unknowns. For instance, it remains to be seen whether patients with cancer will be able to generate antibodies and develop the same protection from the virus as healthy patients. Also unknown is whether there will be unique side effects in this patient population.

"These are things that we will have to learn as we go, and we will," Tripathy said. "As the cancer centers and practices start immunizing their patients, we're going to be tracking their outcomes."

As with any drug that receives FDA approval, there will be a process for reporting and compiling any side effects that occur when a patient receives the vaccine.

As for the two people who developed severe allergic reactions to the Pfizer-BioNTech in the United Kingdom, Chemaly noted that those individuals had a history of anaphylaxis, or severe allergic reactions to different antigens. They already were carrying an EpiPen (epinephrine), which helps combat serious allergic reactions.

"And we're prepared to intervene if someone (develops) this kind of reaction when we give the vaccine," Chemaly said.

SOCIAL DISTANCING, MASKING PRACTICES WILL CONTINUE

Everyone — not just patients with cancer — should follow all the public health measures, including wearing a mask, social distancing and frequent hand washing for at least another six months to one year, even if vaccinated, Chemaly said.

"We need to create herd immunity (because) without herd immunity, we're not going to eliminate this virus," he said. "Second, even if you get a vaccine, (it) doesn't mean you're not going to be exposed to the virus in the community or in your workplace. At that point, you may carry the virus and not get sick from it or get admitted to the hospital … but (you) can still transmit the virus to other people. This is why masking is still so important."

THERE IS NOTHING TO HIDE

Chemaly said he's received questions from patients and employees every day about the vaccines. And although he said that being concerned is understandable, he assures the public that the trials have been conducted under a microscope, meaning many experts have been watching everything that has happened.

"No one is hiding anything," he said. "Based on that, I advise my patients, my colleagues (and) other health care workers in the health care setting that (the vaccines are) safe and are effective. There is no long-term side effect up to two or three months from receiving (a COVID-19) vaccine. I, myself, (felt) very comfortable taking it, and (I lined) up to get the vaccine as soon as it (was) available."

'WITNESSING AN INCREDIBLE MOMENT'

"I think that we are witnessing an incredible moment in history where we rallied to do something that had never been done, and that is to get a vaccine from scratch in less than one year," Tripathy said. "That is a pretty astounding technologic feat that not many people would have believed was possible when all this started — that in this short period of time, we did it."

Now, it's up to patients to make an informed decision as to whether to get a COVID-19 vaccine, although the available data point to their potential effectiveness.

"Nothing works unless you get the vaccine," he said. "If you don't get the vaccine, all of this was for nothing."

However, Tripathy acknowledged that some people may be concerned and reluctant to receive the vaccine.

"Things have happened in medical history where that might give some people pause," he said. "There's a lot of concern about people who are underserved and minorities because there is a history of them not receiving fair treatment when it comes to medicine and clinical trials. And so, we have to go the extra mile to reassure patients. But we can't pretend that we can reassure people 100%. (As with) many other decisions you make in life, you take the best information you have and you make a recommendation for other people or for yourself. All we can do is be truthful, present our recommendations and hope that a majority of people do get vaccinated." C

MIKE KITADA

Adding to the Regimen

The NCCN has updated its recommendations for chronic lymphocytic leukemia and small lymphocytic lymphoma to now include Brukinsa as a first- and second-line therapy in a subgroup of patients. By KRISTIE L. KAHL

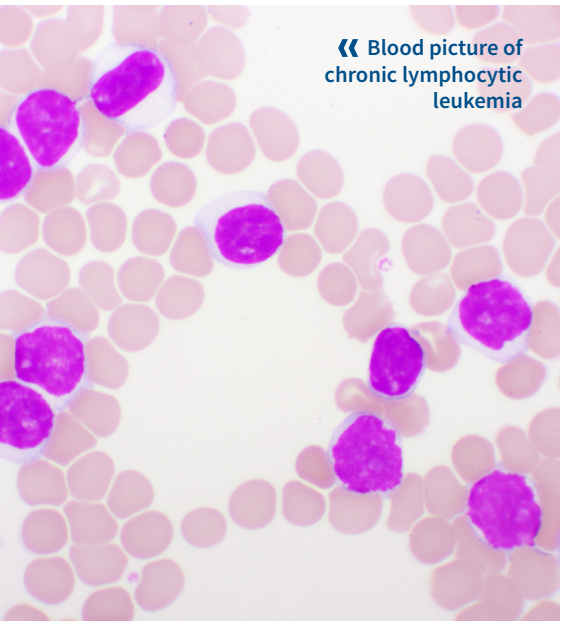
DR. JENNIFER R. BROWN is the director of the Dana-Farber Cancer Institute CLL Center and professor of medicine at Harvard Medical School.

THE NATIONAL COMPREHENSIVE CANCER Network (NCCN) recommended Brukinsa (zanubrutinib), a Bruton tyrosine kinase (BTK) inhibitor, for the treatment of chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL).

Recent NCCN guidelines that were updated on Dec. 3, 2020, now recommend the drug as both a first- and second-line treatment in CLL/SLL, including:

- First-line therapy of Brukinsa as a single agent is recommended for the treatment of CLL/SLL with del(17p) and TP53 gene mutations in patients with a contraindication to other BTK inhibitors who have indications for treatment.
- For second-line treatment and subsequent therapy, the NCCN recommends the indication as a single agent for the treatment of CLL/SLL with or without del(17p) and TP53 mutations in patients with intolerance or contraindication to other BTK inhibitors who have indications for retreatment.

The first-line treatment recommendation was based on results from the phase 3 SEQUOIA study, designed to evaluate Brukinsa monotherapy in treatment-naive patients with CLL or SLL and del(17p). After a follow-up of 21.9 months, patients treated with Brukinsa showed an overall response rate of 94.5%, with a complete response/complete response with incomplete bone marrow recovery rate of 6.4%. Moreover, the 18-month progression-free survival, or the time from treatment to disease progression or worsening, and overall survival rates were 90.6% and 95.4%, respectively.



« Blood picture of chronic lymphocytic leukemia

The BTK inhibitor's tolerability in this study were consistent with what was previously reported. The most common side effects included contusion (20.2%), upper respiratory tract infection (19.3%), diarrhea (17.4%), nausea (14.7%), back pain (13.8%), constipation (13.8%), rash (13.8%), cough (12.8%), neutropenia (11.9%), arthralgia (11.0%) and pneumonia (10.1%).

"BTK inhibitors have demonstrated positive outcomes in CLL or SLL patients with del(17p), who usually respond poorly to standard chemoimmunotherapy, even in the front-line setting," Dr. Jennifer R. Brown, director of the Dana-Farber Cancer Institute CLL Center and professor of medicine at Harvard Medical School, said in a press release issued by BeiGene, the agent's manufacturer.

The second-line treatment recommendation was based on results of a phase 2 trial, designed to evaluate Brukinsa in patients with/without del(17p) and/or TP53 mutations, who have an intolerance or contraindication to other BTK inhibitors. After a median follow-up of 15.1 months, Brukinsa induced an overall response rate of 84.6%. In addition, the 12-month overall response rate was 96% for those treated with Brukinsa. The most common grade 3 or higher side effects seen were neutropenia (44%), thrombocytopenia (15.4%) and lung infection/pneumonia (13.2%).

Brukinsa is a small molecule BTK inhibitor that has been investigated as a single agent and in combination with other agents to treat patients with a wide range of B-cell malignancies. It is currently approved by the Food and Drug Administration for the treatment of adult patients with mantle cell lymphoma (MCL).

The NCCN's recommendation could have two implications for patients with CLL/SLL. First, insurance companies may pay for Brukinsa, in particular, because it is already approved to treat patients with MCL, a closely related blood cancer. However, of note, its use in CLL would be considered off label, as the agent is not approved in this disease state as of yet. On the other hand, the NCCN's recommendation may aid in the FDA's approval of the first- and second-line indications.

BROWN COURTESY OF DANA-FARBER HARVARD CANCER CENTER; LEUKEMIA IMAGE: JARUN011 / STOCK.ADOBE.COM

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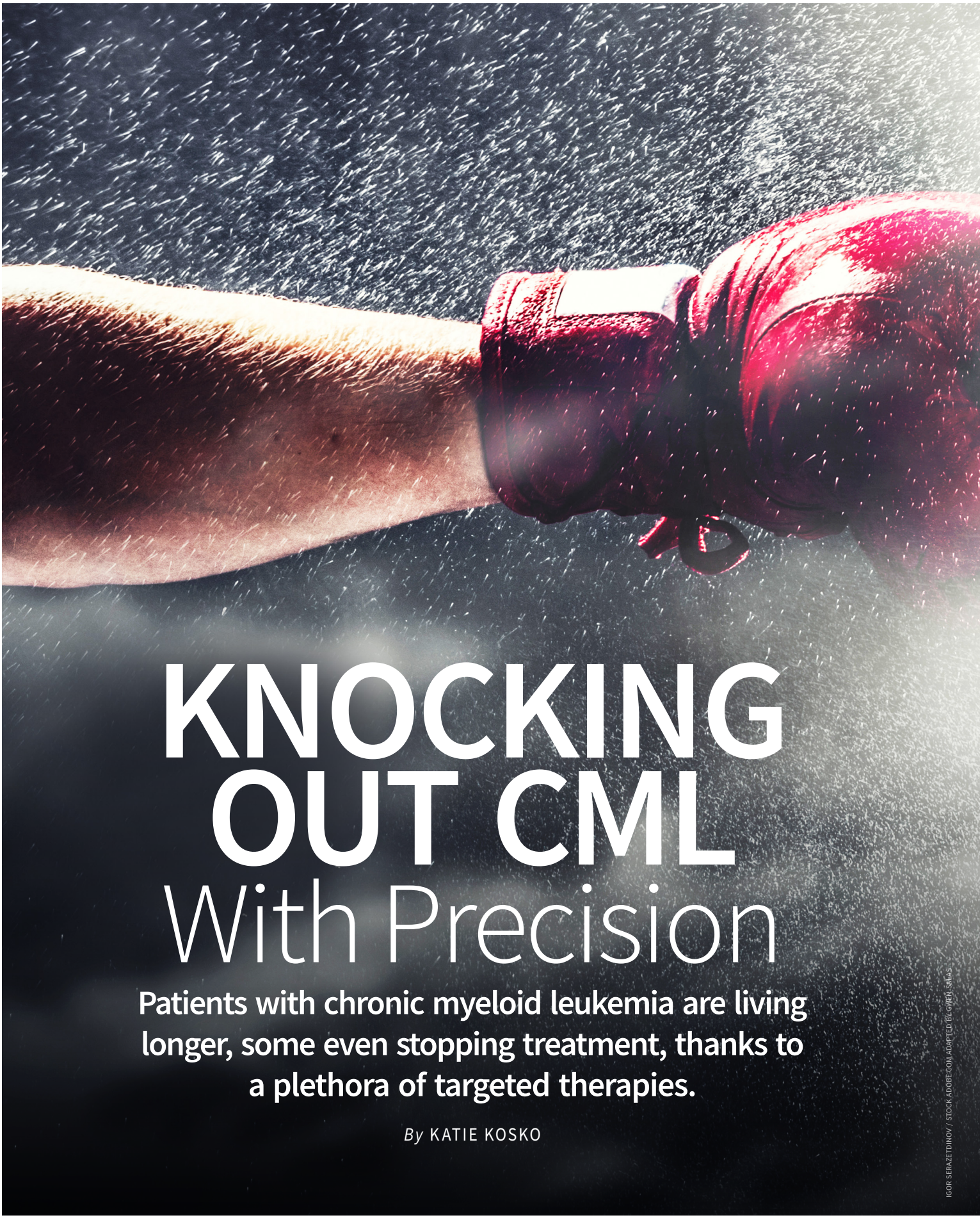

KNOCKING OUT CML With Precision

Patients with chronic myeloid leukemia are living longer, some even stopping treatment, thanks to a plethora of targeted therapies.

By KATIE KOSKO

IGOR SERAZETDINOV / STOCK.ADOBE.COM. ADAPTED BY GWEN SALAS

Mary Sardegna was 2 years old when her parents noticed she wasn't acting like herself. She was fatigued, had no appetite and often developed low-grade fevers. Then her stomach started to grow.

Several doctors thought she might have had the flu, and one suggested an enema to help with her bulging stomach. Eventually, a complete blood count (CBC) was performed, and it showed her white blood cell count was 525,000. A normal range is between 4,000 and 11,000 cells.

That's when Sardegna's parents were told that their daughter had chronic myeloid leukemia (CML), a type of blood cancer in which the bone marrow makes too many white blood cells. The bulge in her stomach was her white blood cells filling up her spleen.

"The only options in 1991 were bone marrow transplant, which had a 3% success rate, or a lifetime of medication," recalls Sardegna, who lives in Laguna Hills, California. "My parents opted for the medication and were told by my doctor, 'You'll be sorry. There is no cure for this cancer. She's going to die.'" »

MARY SARDEGNA received interferon therapy for nine years, getting 70 shots a month.

Sardegna was on interferon therapy for nine years, getting 70 shots a month. By 9 years old, she was injecting herself. "It was keeping the leukemia at bay, but it wasn't helping it," she says. "I was surviving, not thriving." The medication made her tired, sometimes to the point where she would have to crawl across the floor to get to where she needed, and she developed a speech delay and learning disability.

"When I was in fourth grade, my mom got onto the internet — this was when it started to first come out — and she found a chat room where people were talking about a pill, STI-571. My pediatric oncologist had never heard of it," Sardegna says.

STI-571 is now known as Gleevec (imatinib), a tyrosine kinase inhibitor (TKI) that targets BCR-ABL. This gene is formed on chromosome 22 when it fuses with chromosome 9; the abnormal chromosome is called the Philadelphia chromosome — a signature genetic aspect found in all patients with CML.

After researching the then-investigational drug, Sardegna's mother found out about a clinical trial being conducted in Portland, Oregon, by Dr. Brian Druker in patients with CML. In 2001, they flew to Portland, and 11-year-old Sardegna became one of the few children allowed on the trial.

"Within nine months, I was considered cancer free," she says. "I was less tired. I could walk and talk. I was thriving."

Treatment advancements helped Sardegna, now 31, defy the odds. She was able to graduate college, get married and hold a job as a professional nanny. In January 2019, after 19 years on Gleevec, Sardegna safely came off treatment.

THE POWER OF FIVE

Targeted therapies like Gleevec, the first Food and Drug Administration (FDA)-approved TKI for CML, have not only transformed treatment but also turned the once-deadly disease into a condition that can be managed.

In addition to Gleevec, a first-generation TKI, four others are approved by the FDA: Bosulif (bosutinib), Sprycel (dasatinib) and Tasigna (nilotinib), all second-generation TKIs; and most recently, Iclusig (ponatinib), a third-generation TKI.

"Before we had TKI or stem cell transplant, the average life expectancy was seven years," says Dr. Jerald Radich, a medical oncologist at Fred Hutchinson Cancer Research Center in Seattle. "With (these) new agents, life expectancy is pretty much normal."

Unlike acute leukemias, CML is slow growing, survival is longer and about 80% to 85% of cases are diagnosed incidentally during routine bloodwork, according to Dr. Jorge Cortes, director of the Georgia Cancer Center at Augusta University in Augusta, Georgia.

Often, patients don't know they have cancer lurking inside their body because symptoms aren't obvious and they mimic other conditions. CML may cause fatigue, weakness, bone pain, fever and loss of appetite.

Joan Clements experienced all of the above. In 2000, she was caring for her husband who recently had had surgery and helped her mother move from Arizona to California, so she wasn't focused on her own health. She just knew something wasn't right. While carrying boxes in the moving process, Clements noticed bruising on her body. That's when she made herself a doctor's appointment and brought him a list of 14 signs of leukemia. However, when she received the results of her blood test, the nurse told her everything looked fine.

Clements got sicker, dropping 28 pounds in just under two weeks. She demanded a CT scan with full contrast. But before she could proceed with the procedure, she needed bloodwork. "When I got home that day, my phone was ringing and it was the doctor saying, 'You have to come back to the hospital right now,'" says Clements, now 78, who lives in Costa Mesa, California. "My white blood cell count was 375,000."

Clements, then 59 years old, learned she had CML and was told she had two to four years to live because there was no cure. Instead of waiting helplessly, she went to City of

NATALIE MOSER

Hope Comprehensive Cancer Center in Duarte, California. That's where she learned about Gleevec. "I said, 'I want this drug. I'm going to fight this beast,'" she recalls.

Clements celebrated her 19-year "cancer-versary" in December. She's thankful to still be alive because of Gleevec, which she will remain on for the rest of her life, but it didn't come without unpleasant side effects, such as nausea, vomiting, fatigue, gastrointestinal issues, leg cramps, brain fog, full body rashes and periorbital edema, or swelling around the eyes. "It looked like water balloons on my eyes," says Clements, who co-founded the CML Buster Foundation and leads its U.S.-based CML Busters family support group. Although many of these side effects are common when first taking TKIs, in Clement's case, most subsided and the ones that remain — gastrointestinal issues, nausea and brain fog — are manageable.

Compared with chemotherapy, targeted therapy is more effective and typically has fewer side effects. "Chemotherapy is a bomb. You throw it and try to kill all the bad guys," explains Cortes. "These targeted therapies are specifically directed to where the bad guys are to spare the good. It's more precise."

TKIs are given as initial treatment for patients, and the advantage to having so many is that if a patient doesn't respond to one, the dose can be increased or they can switch TKIs. For those who can't take TKIs, interferon or chemotherapy may be used. And, although patients with chronic phase disease are rarely treated with stem cell transplants, that may be an option, especially for younger patients.

When deciding how to treat a patient, an oncologist takes into account many factors, such as comorbidities, schedule, cost, age and whether the patient is of childbearing age.

In three randomized studies, second-generation TKIs were compared with Gleevec, and there is no difference in overall survival, according to Radich. However, second-generation drugs achieve a deeper response more quickly, and they tend to have less disease progression to an advanced phase.

"If you have an older patient and aren't worried about them going into advance phase or having kids, then you would go with imatinib," says Radich. "If it's chronic phase, but the patient has a big spleen and has been sick or is younger and they want a response so they can get off drug, they might be good for second-generation TKIs."

Monitoring patients regularly in CML is common to see how well therapy is working. A polymerase chain reaction test is typically done every three months by blood or bone marrow, and it looks for molecular responses — seeing the number of leukemia cells. Hematologic responses can be measured through a CBC to make sure blood cell levels return to normal. To test for a cytogenic response, or examining mutated chromosomes, a doctor can use a bone marrow sample.

WHAT'S IN THE PIPELINE?

Although there is an abundance of treatment choices for patients with CML, researchers are always looking for something better. »

"When I got home that day, my phone was ringing and it was the doctor saying, 'You have to come back to the hospital right now.' My white blood cell count was 375,000."

— JOAN CLEMENTS

» JOAN CLEMENTS celebrated her 19-year "cancer-versary" in December.

NATALIE MOSER

ANGELINA SHILCOSKY; HER HUSBAND, DAN; and her sons **ETHAN (RIGHT)** and **Isaiah.**

"Several medications are in development to address specific resistance, a mutation called T315I, and the most significant development is a targeted drug that is similar to the available therapies, but it has a unique mechanism of inhibition," says Dr. Michael Mauro, a hematologist at Memorial Sloan Kettering Cancer Center in New York City.

That drug is called asciminib (ABL001), and it targets the ABL myristoyl pocket. It's known as a STAMP inhibitor. Results of a phase 3 clinical trial showed that the therapy was safe and improved response rates over current options. Experts anticipate it to be approved by the FDA this year.

"Sometimes the mutations don't allow the TKI to find its place where it can do its job," Cortes explains. "By binding in a different place, which asciminib does, it allows it to work and override the resistance."

A medication being developed in China, HQP1351, is being examined for its efficacy. Its focus is zeroing in on the T3151 mutation, and it could potentially be a therapy for those with CML whose disease becomes resistant to a first- or second-generation TKI.

In a phase 1 study, the drug K0706 has shown to be safe in patients who have received at least three prior lines of TKI therapy. It's effective against wild-type and mutated BCR-ABL1 proteins.

And in Russia, researchers are examining PF-114, which also has activity against the T3151 mutation, and has shown good responses.

ACHIEVING TREATMENT-FREE REMISSION

However, maybe most remarkable in the evolution of CML therapy is the emerging goal for patients to enter treatment-free remission, or TFR. It's a decision that isn't taken lightly.

In Sardegna's case, when she asked her oncologist about it, she wasn't met with open arms. Sardegna reached out to Druker, who has become a lifelong friend, for a second opinion, and he felt she was a great candidate.

To be considered for TFR, patients must reach a deep molecular response, which is defined as four to five reductions in disease burden, Radich explains. This needs to be sustained for at least two years.

Only about 40% to 45% of patients can stop treatment safely, according to Cortes, and about half will relapse.

Patients are monitored every month for the first six months with routine blood tests. Then follow-ups go down to every two to three months for the next two years, Mauro explains.

In September, Angelina Shilcosky was asked by her doctor whether she wanted to stop therapy because she had been in complete remission for a few years. "I was nervous at first, but it took stress off my mind," says Shilcosky, 43, who received a CML diagnosis at 27 when she was three months pregnant and had a 2-year-old at home. "My mom and mother-in-law told me to stay on it. But I trust my oncologist, and he said if numbers (started) to change, we (would) go back on it."

Shilcosky feels like she's forgetting to do something each night because she popped a Gleevec pill daily for 14 years, but she feels thankful to be off it and gives back to the CML community by participating in the Leukemia & Lymphoma Society's Light the Night campaign each year.

A downside to TFR is the potential for withdrawal symptoms, which Sardegna experienced. "Around six months after I stopped treatment, I got excruciating muscle pain," she says. "It felt like my muscles were turning over."

About 10% to 30% of patients who stop TKI therapy report withdrawal symptoms like bone pain and/or rash. However, most can be managed through over-the-counter medications, according to the Leukemia & Lymphoma Society.

"It's important to remember that it's a marathon, not a sprint," Mauro says. "But it should be one where side effects are minimal and response is on target hitting milestones."

COURTESY OF ANGELINA SHILCOSKY

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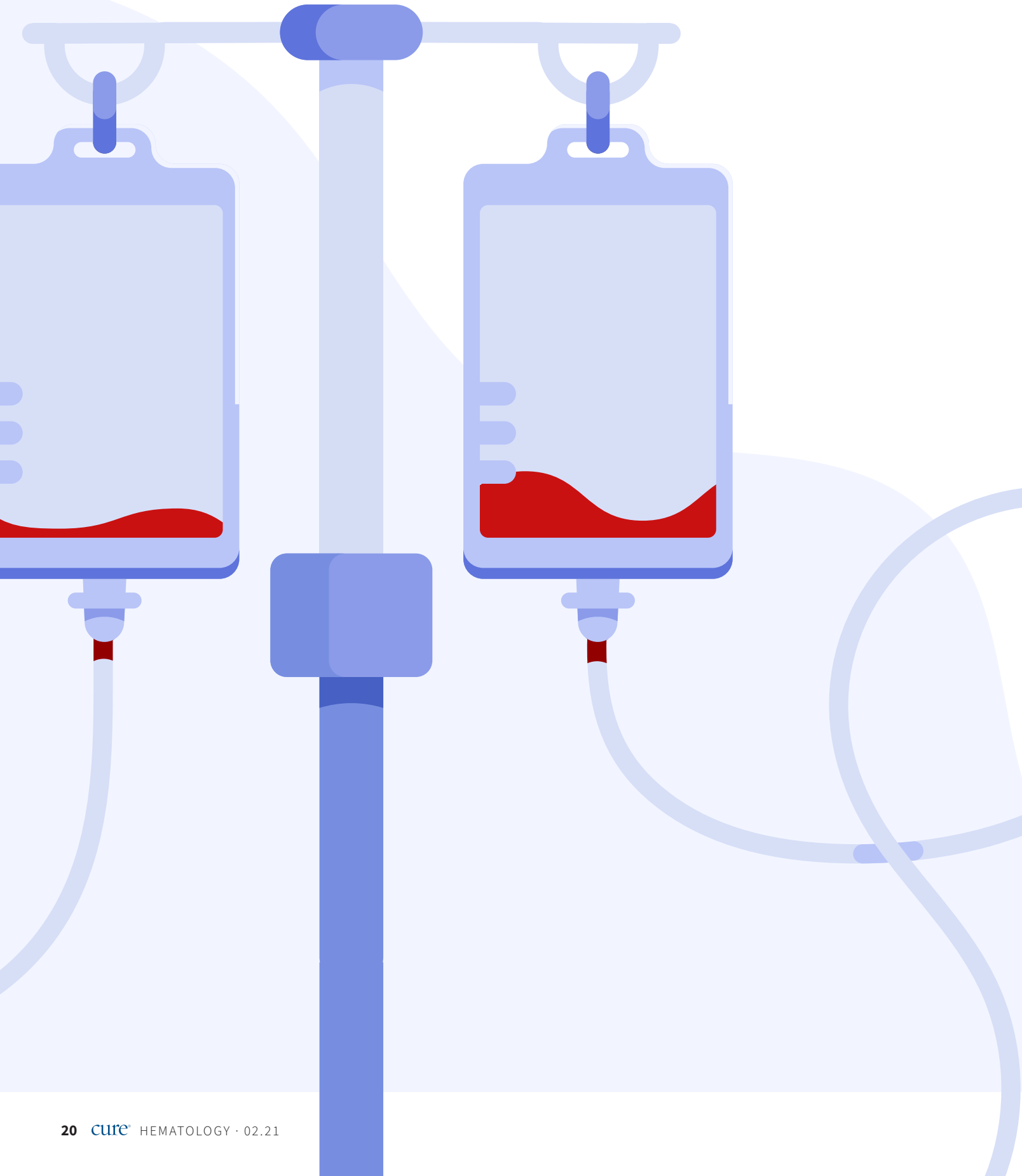

KEEP IT Flowing

Combating COVID-19 Blood Shortages

Blood shortages during the COVID-19 pandemic have forced cancer centers to get creative to ensure patients with hematologic malignancies are able to get transfusions in a timely manner.

By ARLENE WEINTRAUB

When Marie Fuesel was treated for leukemia eight years ago, she needed donated blood products more than 100 times.

"They'd give me my chemotherapy, I'd stay in the hospital for a week, then I'd go home, get really sick and have to come back in for blood and platelets," says Fuesel, 53, a retired insurance agent who lives in suburban Chicago. "I spent over 100 days in the hospital over eight months. The disease and treatments (affect the bone marrow and production of red and white blood cells and platelets), so many transfusions were required to achieve remission."

After eight months of chemotherapy, followed by a year on the targeted drug Sprycel (dasatinib) as part of a clinical trial, Fuesel went into remission. She no longer needs transfusions, but she still appreciates the need for blood donors. "I wouldn't be alive if the blood wasn't available when it was needed," she says. »

IRINA SHATILOVA / STOCK.ADOBE.COM ADAPTED BY GWEN SALAS

» **MARIE FUESEL** needed blood products more than 100 times during treatment

Back then, blood shortages weren’t common, but they are now. The stay-at-home orders at the beginning of the COVID-19 pandemic forced the cancellation of numerous blood drives, and safety concerns arising from its spread have prompted some frequent donors to stay away from donation centers.

That’s been a source of worry for oncologists. Patients with cancer use nearly one-quarter of the nation’s blood supply, according to the American Red Cross, and donated blood is a vital resource in the treatment of hematologic cancers. Patients who receive stem cell transplants often need transfusions of oxygen-carrying red blood cells, infection-fighting white blood cells and platelets to control bleeding. Blood transfusions are common in the supportive care of patients undergoing chemotherapy that suppresses production of all the blood cells that results in anemia, because they relieve symptoms that ensue, such as fatigue and shortness of breath.

Between March and June 2020, 37,000 blood drives were canceled, according to the American Red Cross. The impact of the blood shortage varied across the nation but has hit some cities particularly hard. The New York Blood Center, for example, which supplies New York City hospitals, reported in December 2020 that it had just three days of supply on hand, down from the five- to seven-day supply it normally has.

Ongoing shortages are forcing cancer centers to change some of their procedures for using donated blood. “We all recognize that we are in the midst of a public health crisis and that we all have to do our part,” says Dr. Mikkael Sekeres, chief of hematology at the University of Miami Miller School of Medicine and a physician liaison in hematology at Sylvester Comprehensive Cancer Center.

TWEAKING TRANSFUSION THRESHOLDS

In response to COVID-related blood shortages, several cancer centers adjusted their policies for transfusing blood. Moffitt Cancer Center in Tampa, Florida, for example, developed a blood shortage action plan, according to Dr. Kaaron Benson, director of the blood bank at Moffitt. “It basically meant dropping some of the thresholds we would normally use for transfusion,” Benson says.

Moffitt has not needed to implement the plan yet, but if it does, Benson says, the change would most likely have the biggest effect on patients with leukemia and lymphoma who are given platelets as a preventive

LAURIE PEACOCK

strategy. "Provided they're not bleeding or engaging in activities that increase the risk of bleeding, studies have shown you can allow the platelet threshold to drop from our standard of 10,000 per microliter to 5,000," she says.

The technique was first suggested in a 1991 journal article and has since been widely accepted as an appropriate change to make during blood shortages, Benson says.

In recent years, many oncologists have set lower thresholds for red blood cell transfusions — another change that has eased the strain on blood supply. They used to routinely order transfusions for patients with hemoglobin levels below 10 grams per deciliter. That number dropped to between 7 and 8 grams per deciliter after a series of studies showed that infusing red blood cells at the higher threshold did not improve treatment outcomes.

> **"We all recognize that we are in the midst of a public health crisis and that we all have to do our part."**
>
> — *DR. MIKKAEL SEKERES*

During the pandemic, Moffitt and other cancer centers are also delaying some stem cell transplants and elective surgeries, so that blood used during those procedures can be kept on hand for patients who urgently need it, such as trauma patients or those needing emergent surgery. But those decisions are made on a case-by-case basis, so patients should maintain a frequent dialogue with their oncologists to determine the best plan for managing their symptoms during the pandemic.

Patients with multiple myeloma, for example, can benefit from stem cell transplants, but it's usually not urgent, says Dr. Stephanie Lee, a hematologist and professor at the Fred Hutchinson Cancer Research Center in Seattle. "We have very good treatments for multiple myeloma, so we can continue to give patients chemotherapy for weeks or months," Lee says.

However, she explains, patients with leukemia who need stem cell transplants may be advised to undergo the procedure as quickly as possible, even during the pandemic, because delaying it could cause the cancer to grow and become resistant to treatment.

And some patients with cancer who are simultaneously fighting other diseases should receive all the blood and platelet transfusions they need to manage their cancer, as well as to address any risks posed by chronic conditions. "If you have heart disease, and your hemoglobin drops even further, you're more likely to get angina or suffer a heart attack," Sekeres says. "So, for those people with serious comorbidities, we are more aggressive in transfusing blood products."

GROWING THE DONOR POOL

Stephenie Perry, who works as the business operations coordinator for the American Red Cross of Northwest Georgia, knows firsthand the value of donated blood. Perry is a survivor of Hodgkin lymphoma who needed several transfusions during her treatment, which consisted of a round of chemotherapy and two stem cell transplants.

LAURIE PEACOCK

MARIE FUESEL helped run the seventh annual Great Chicago Blood Drive in January, and more than 2,000 units of blood were collected.

Perry, 31, has been in remission since February 2018, but sometimes her red blood cell count still runs low and she needs another blood transfusion. "I feel sluggish, and when I stand up, I get really dizzy," says Perry, who lives in Rome, Georgia. "When I get a transfusion, it's like someone has just given me a shot of energy."

How can patients adapt when blood shortages mandate less frequent transfusions? Lifestyle changes can make a big difference, Sekeres says. "If a patient is becoming progressively anemic, and it's someone who usually goes for a 2-mile »

STEPHENIE PERRY, a survivor of Hodgkin lymphoma, needed several transfusions during treatment.

walk every day, maybe they'll reduce it to 1 mile or cut (exercise) altogether," he says.

Some patients may be eligible for iron infusions, which can relieve symptoms of fatigue and lengthen the period between infusions, says Abbey Fueger, clinical trial nurse navigator for the Leukemia & Lymphoma Society.

In addition, there are other small changes that can lessen the risk of anemia and improve symptoms. "Some physicians are trying to limit blood draws for patients and recommending nutritional supplements that might help them feel better and lengthen the time between infusions," she says.

Meanwhile, an effort is underway to expand the pool of potential blood donors. In April, the Food and Drug Administration (FDA) addressed blood shortages brought on by COVID-19 by easing up on some of its restrictions on who can donate. For example, people who are at risk of contracting HIV, and those who have a recent tattoo or piercing or possible exposure to an infected individual no longer have to wait one year to give blood. The new waiting period is three months.

The FDA also dropped the waiting period for donors who have traveled to malaria-endemic countries from one year to three months. And it no longer recommends that blood centers turn away donors who lived in certain European countries during the era when Creutzfeldt-Jakob disease, a rare and fatal degenerative brain disorder, was thought to be spreading.

The hospital community is rallying around the cause, holding blood drives of their own and encouraging family members of patients to donate blood.

During the first few months of the pandemic, Fuesel helped put together five small blood drives in her town of Orland Park, Illinois. They were so successful the American Red Cross and a local news broadcaster asked her to help run the seventh annual Great Chicago Blood Drive. So, she did, and on Jan. 13, that event collected 330 units of blood at the Orland Park location and more than 2,000 units at other drives around the city.

For donors who might be nervous about giving blood during a pandemic, Fuesel has a message: It's safe and important. "All the beds are spaced apart, and there are different stations when you walk in for getting your temperature checked and using hand sanitizer," Fuesel says. "I know these are hard times, but it doesn't cost anything to give your blood. It's a way to help."

CHRIS HAMILTON, AMERICAN RED CROSS

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KEITH OWENS went to the hospital for bloodwork and left one month later.

CAROLE VOLPE

A T-ALL Order

Oncologists and researchers are racing to identify new therapies to help better treat a rare form of acute lymphoblastic leukemia.

By ERIK NESS

Keith Owens had no time to be sick.

He and his wife were driving home from a late July wedding in 2019 when it really began to hit him. Back in Rochester, New York, he collapsed, and then endured three days of chest pains, a terrible cough and night sweats. He barely left his bed. "Everything started to seem a little bit harder to me," he says. "I've always kind of overexerted myself with everything I do. Just thought I was overworking myself."

Owens' wife, Allison, was eight months pregnant. Like many other 31-year-olds, Owens didn't even have a doctor. But once Allison dragged him to urgent care, things escalated quickly. His blood pressure was through the roof. Another doctor suspected thyroid issues and ordered imaging, which revealed a 6-inch mass in his chest. Owens headed to the hospital for bloodwork and didn't check out for a month. »

For many cancers, diagnosis unfolds at what feels like a glacial pace. Weeks elapse between appointments. There's ample opportunity for research, worry and second opinions. But T-cell acute lymphoblastic leukemia (T-ALL) hits like a landslide.

"In most instances, it is a very urgent situation where we need to hospitalize people and get them going on treatment," says Dr. Mark Litzow, head of the acute leukemia group at Mayo Clinic in Rochester, Minnesota.

"All these procedures are coming at them," says Owens' oncologist, Dr. Kristen O'Dwyer. She's clinical director of the acute leukemia program of the Wilmot Cancer Institute at the University of Rochester Medical Center in New York. "I have to do a bone marrow biopsy, get a central line and a lumbar puncture, an echocardiogram. If it's a young man, there's fertility preservation. All these things in a matter of 48 hours, so I can get them starting on treatment. And they have to trust me," O'Dwyer adds, "which is huge, especially for a young patient who is like, 'I don't have cancer. I've just been really tired because work has been crazy.'"

CURE RATES DECLINE AS PATIENTS GET OLDER

Acute lymphoblastic leukemia (ALL) — sometimes known as acute lymphocytic leukemia — is an aggressive cancer of the blood and bone marrow. "Our bone marrow produces many billions of cells every day," says Litzow. Stem cells in the marrow produce immature cells called blasts that, when healthy, will develop into one of many different blood cells. In this constant state of division, mistakes happen. Biological safety mechanisms catch most of these, but sometimes abnormal cells escape and take over. "Instead of maturing and producing red blood cells, white blood cells and platelets, it just keeps making more of itself," Litzow says.

> **"Everything started to seem a little bit harder to me. I've always kind of overexerted myself with everything I do. Just thought I was overworking myself."**
>
> *— KEITH OWENS*

Most ALL (85%) derives from defects in B lymphocytes, cells that normally mature into the antibody-producing white cells that help fight off infection. Cure rates for B-ALL are high and getting higher. T-ALL arises from T lymphocytes, which are important cells in the immune system for fighting infections and other immune functions.

The most common childhood cancer, ALL also afflicts adults. T-ALL is a subset of ALL and is a rare cancer: An estimated 6,150 new cases of ALL were diagnosed in 2020 in the United States; just 25% of these cases were in adults with T-ALL. It's largely a disease of adolescents and young adults (aged 15 to 39). Although incidence diminishes with age, it's a trade-off: Cure rates for children are high and decline as patients get older.

In young children, certain genetic mutations found in B-ALL tend toward good outcomes. In teenagers, these "good" mutations decline and high-risk elements gain. "By the time you're looking at young adults, you very rarely see the good-risk genetic subtypes," says Dr. Stephen Hunger, director of the Center for Childhood Cancer Research at the Children's Hospital of Philadelphia. "The high-risk genetic subtypes are much more common."

Treatments began to emerge for ALL in the late 1960s. When some patients recovered from early-generation chemotherapy regimens and others did not, doctors learned from the differences. Children, for example, did better than adults. In the 1970s it became possible to distinguish between ALL from B lymphocytes and T lymphocytes. The more common B-ALL responded well to therapy, while patients with T-ALL fared much worse.

Treatment for B-ALL delivered on this promise and has reached exceptional levels thanks to new antibody therapy and CAR-T cell therapy. Treatments for T-ALL have not kept pace, though in the past few years improvements have led to cure rates approaching 90% in children and 70% in young adults.

ALL treatments are relatively similar, with one big difference: If the first line of treatment fails, backup for T-ALL is very limited, with Arranon (nelarabine) being administered with mixed results in patients. "For patients who do not achieve remission, or (who) relapse after achieving remission, it is nearly impossible to find an effective treatment," says O'Dwyer.

TWO SCHOOLS OF THOUGHT

T-ALL treatment regimens are difficult and complex, and adapted to a patient's individual risk. Patients with a better prognosis need less intensive therapy, while those with less favorable prospects require more intensive treatments. "We're trying to get a balance between avoiding toxicity and maximizing cure rates," Hunger explains.

For T-ALL, the therapeutic regimens may include a half dozen or more drugs. Many of these specifically target the cancer — cyclophosphamide, vincristine sulfate, Adriamycin (doxorubicin), daunorubicin, cytarabine, mercaptopurine, thioguanine and Oncaspar (pegaspargase). Steroids like prednisone and dexamethasone are used liberally, as they are directly toxic to lymphocytes and therefore slow the disease and influence the immune system in useful ways. Other agents offer more immune modulation and help dampen side effects like neurotoxicity.

Some are given intravenously and others orally; a few are delivered both ways at different times. It's often hyperfractionated, which means smaller doses are given at shorter intervals. Intrathecal therapy — fed into the spinal fluid via lumbar puncture — is used in all patients to prevent central nervous system relapse. Radiation is also possible

for pockets of disease in places like the testicles where chemotherapy does not penetrate well.

A patient will typically experience many of these in a rotation of therapeutic cocktails that typically last 2.5 years. After diagnosis, there's typically a monthlong hospital stay. Called induction, its goal is to hit the cancer hard and induce remission, while closely monitoring results.

How the cancer responds to treatment is pivotal, and the ultimate measure of patient response is called minimal residual disease (MRD). By taking a bone marrow sample and using high-tech scanners, it's possible to detect minute levels of malignant blast cells. The more blast cells, the higher the risk of relapse. It's an important metric, because how patients respond to the initial therapy is very predictive of the likelihood of successful treatment.

After induction, the next phase, known as consolidation, can last from eight months to more than a year. Some courses during this time are very intense — many consecutive days of treatment — while others are devoted to recovery. Some patients receive a stem cell transplant, a challenging round of treatment, immune isolation and recovery all by itself. The last year to 18 months is maintenance therapy, typically delivered orally.

Two different schools of practice have emerged for how to combine and sequence these treatments. They use similar ideas and ingredients, but are assembled in slightly different ways, as oncologists have strong preferences based on training and experience.

The two regimens go by the clumsy names hyper-CVAD and augmented Berlin-Frankfurt-Münster (aBFM). Because of the acute nature of T-ALL and the length of treatment, a patient's treatment may be limited to the regimen practiced by their provider.

O'Dwyer says aBFM is common in most academic cancer centers. Hyper-CVAD, meanwhile, is more commonly used in community oncology, with the notable exception of The University of Texas MD Anderson Cancer Center in Houston. "They're always doing a hyper-CVAD," she says. "The results are, of course, excellent."

But O'Dwyer has some opinions about the limits of hyper-CVAD in a community setting, where it is often used to treat both B-ALL and T-ALL, along with other blood cancers. Because T-ALL is rare, her concern is the lack of experience with some of the more complicated elements, like administering Oncaspar, an enzyme that breaks down a key amino acid fueling leukemia cell growth. It's a difficult drug because of side effects — infusion reactions, severe toxicities, blood clots and pancreatitis. Experience helps guide safe use. "It's such an important component for the cure of this disease that it's really required," she says.

Intrathecal therapy is also a challenge for those who don't deliver it regularly. "We can get it done efficiently and quickly and safely. It's harder to do that in the community," O'Dwyer says. So that her patients can travel less, she partners with community oncologists for more straightforward aspects of treatment and handles the more complex elements in house.

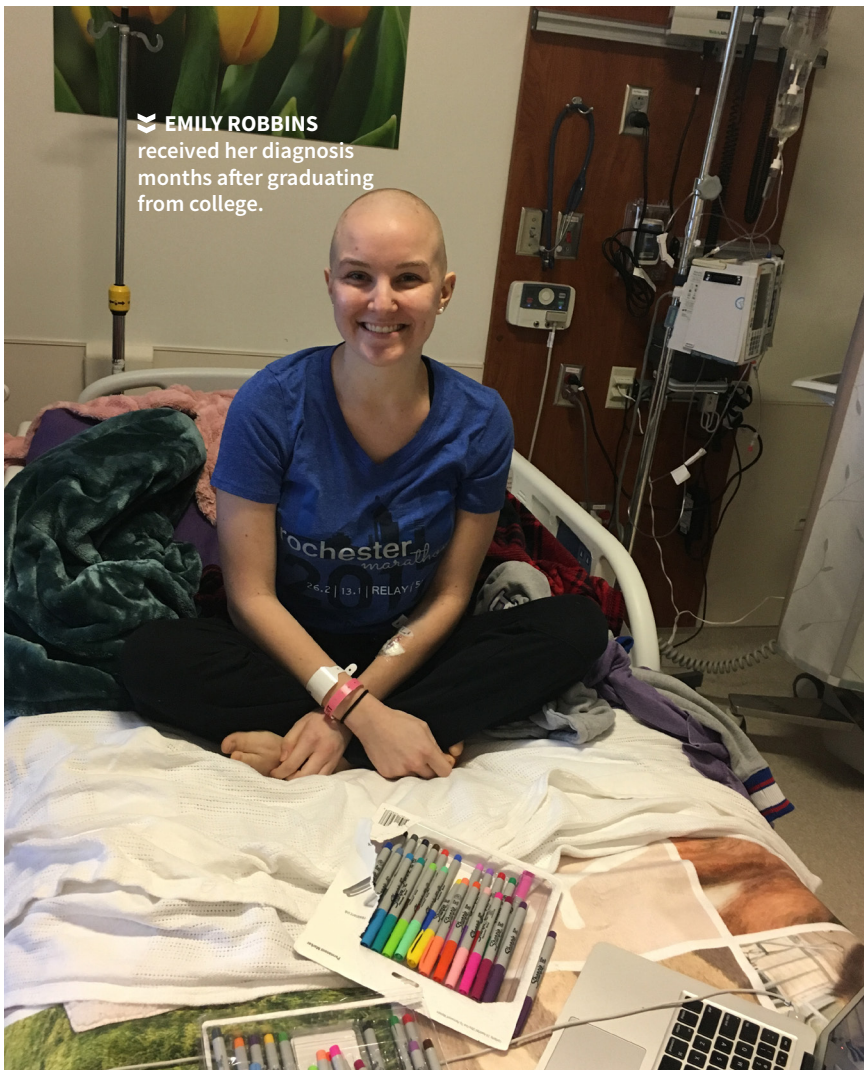
"The plan should be developed in discussion with someone who does this a lot," says O'Dwyer. "I think T-ALL is rare enough that, when at all possible, patients should be referred. It's high stakes, upfront. You want to get it right the first time because you have so little salvage option."

NEW STANDARD OF CARE

Emily Robbins was 22 when a lump in her neck knocked her world off track. In the previous few months, she'd run her first full marathon, had graduated from college and was barely into the second month of her first full-time job. Even as she was wheeled into the Wilmot Cancer Institute, she could not fathom the diagnosis. "I guess my body just didn't want to hear that," she says.

Robbins is not a child, but she has been treated as one — and that's a good thing, because children tend to do better in ALL generally. Partly that's due to favorable genetics, but partly it's because they handle the difficult regimen better.

But as oncologists have gotten better at delivering their difficult medicine and managing side effects, they've pushed the treatment limits to extend pediatric treatment »



EMILY ROBBINS received her diagnosis months after graduating from college.

PHOTO COURTESY OF EMILY ROBBINS

EMILY ROBBINS says she can't imagine anyone younger than her going through such intense treatment.

to adults. Results of a rigorous trial consisting of 295 patients, ranging in age from 17 to 39 years, were published in 2019. Only 3% of patients died of treatment-related causes, and only two patients died after remission. Just as important, the amount of time before complications occurred almost doubled, to 6.5 years.

This new standard of care, which is also a new framework for future research, had been reported in a national meeting shortly before Robbins got sick and was the model for her treatment. But it's not child's play. The first month of hospital-based treatment was rough, though not in the same way as she had imagined. "I slept almost all day," she says. "What was really hard was how weak my body got." Because of the length of the treatment, she says, the side effects and the drugs that caused them all blend together for her.

While many children go back to school during the maintenance phase and resume a normal life, the oral chemo caused nausea for Robbins. She tried to return to work, but it didn't go well. She was still tired and had lots of side effects. "I pushed myself too hard," she says. "My advice would be just to give yourself a break."

The length of treatment really defines the experience. "I don't know what normal is," she says. "I don't remember. I can't compare my life to what normal was for me. I can't imagine anyone younger going through it. Thinking of someone young having to get that kind of intense treatment is just scary to think about."

"We've done a lot to improve cure rates for T-ALL, which is very rewarding," says Hunger. "But you know, it's still pretty nasty treatment that you wouldn't wish on your worst enemy. The upper age limit for who will tolerate those regimens is a bit of a moving target. Certainly, at the age of 40, we definitely would consider — unless somebody had a lot of other medical problems — giving a pediatric-intensive regimen." But as T-ALL occurs in patients past their 50s, the outcomes decline. They have higher-risk disease, don't tolerate the aggressive treatment as well and have a higher risk of complications.

POTENTIAL DEVELOPMENTS

For many cancers, the enormous strides in the ability to read genetic code have unlocked a range of new therapies. However, those targets have led to a dead end. "They haven't translated into clinical use at all," says O'Dwyer.

Indeed, the latest improvement comes from Arranon, a drug first conceived of in the 1950s, then brought to fruition in the 1970s. Arranon inserts itself into T-cell DNA when it gets copied. The error triggers cellular self-destruction. It was first approved in 2005 for patients who had failed two rounds of conventional treatment.

But Arranon has serious and sometimes fatal neurologic toxicities. "It was a hard drug to move forward," says Hunger, who was involved in the clinical trials. "We had to go through nearly a decade of studies just to first prove to ourselves and everybody else that it was safe to give to patients." Eighty percent to 85% of patients are cured without it and 85% to 90% are cured with it. "Clearly it improves the overall outcome, but only marginally, which is most of what we're looking at these days," he says. "These advances take place because patients decide to trust physicians and enroll in clinical trials to test new therapies. It's a partnership between patients and physicians."

CAR-T cell therapy, the much-heralded new immunotherapy, has provided unprecedented remission rates for patients with B-ALL. T-ALL has been more puzzling because the therapy manipulates the very same T cells that go haywire. With the cancer intimately entangled in the biology of the cure, wires get crossed, and the wrong T cells get killed. Scientists are working on solutions, and O'Dwyer expects a lot more patients to be treated for T-cell malignancies at various research hospitals this year.

Despite the promise of CAR-T cell therapies, the next round of trials toward incremental improvement in standard therapy is being shaped now, building off the Arranon-enhanced pediatric regimen.

Among the agents on the near horizon are Velcade (bortezomib), Darzalex (daratumumab) and a tag team of Venclexta (venetoclax) and navitoclax. Velcade is already used to treat multiple myeloma and mantle cell lymphoma, and other blood cancers. Like many chemotherapy agents, Velcade triggers natural self-destruct sequences common to all cells.

Darzalex is also used in the treatment of multiple myeloma and several rare lymphomas. It targets CD38, a protein common on T-ALL cells. Venclexta has already been approved for use in chronic lymphocytic leukemia.

O'Dwyer and her colleagues are hoping to test Darzalex and Venclexta/navitoclax in parallel, flipping patients from one treatment to the other depending on results. "We'll get a lot of information based on those two approaches," she says.

PHOTO COURTESY OF EMILY ROBBINS

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CALQUENCE is a prescription oral treatment for adults with chronic lymphocytic leukemia or small lymphocytic lymphoma. May cause serious side effects including: serious infections, bleeding problems, decrease in blood cell count, new cancers, and heart rhythm problems. Some may lead to death. Tell your doctor if you experience infections such as flu-like symptoms; unexpected bleeding such as blood in your stool or urine; or heart rhythm problems such as fast or irregular heartbeat. Use sun protection when outside.

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CALQUENCE is a prescription medicine used to treat adults with:

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It is not known if CALQUENCE is safe and effective in children.

Before taking CALQUENCE, tell your healthcare provider about all of your medical conditions, including if you:

- have had recent surgery or plan to have surgery. Your healthcare provider may stop CALQUENCE for any planned medical, surgical, or dental procedure.
- have bleeding problems.
- have or had heart rhythm problems.
- have an infection.
- have or had liver problems, including hepatitis B virus (HBV) infection.
- are pregnant or plan to become pregnant. CALQUENCE may harm your unborn baby and problems during childbirth (dystocia).
  - If you are able to become pregnant, your healthcare provider may do a pregnancy test before you start treatment with CALQUENCE
  - Females who are able to become pregnant should use effective birth control (contraception) during treatment with CALQUENCE and for at least 1 week after the last dose of CALQUENCE.
- are breastfeeding or plan to breastfeed. It is not known if CALQUENCE passes into your breast milk. Do not breastfeed during treatment with CALQUENCE and for at least 2 weeks after your final dose of CALQUENCE.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking CALQUENCE with certain other medications may affect how CALQUENCE works and can cause side effects. Especially tell your healthcare provider if you take a blood thinner medicine.

How should I take CALQUENCE?

- Take CALQUENCE exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking CALQUENCE unless your healthcare provider tells you to.
- Your healthcare provider may tell you to decrease your dose, temporarily stop, or completely stop taking CALQUENCE if you develop certain side effects.
- Take CALQUENCE 2 times a day (about 12 hours apart).

(continued)

- Take CALQUENCE with or without food.
- Swallow CALQUENCE capsules whole with a glass of water. Do not open, break, or chew capsules.
- If you need to take an antacid medicine, take it either 2 hours before or 2 hours after you take CALQUENCE.
- If you need to take certain other medicines called acid reducers (H-2 receptor blockers), take CALQUENCE 2 hours before the acid reducer medicine.
- If you miss a dose of CALQUENCE, take it as soon as you remember. If it is more than 3 hours past your usual dosing time, skip the missed dose and take your next dose of CALQUENCE at your regularly scheduled time. Do not take an extra dose to make up for a missed dose.

What are the possible side effects of CALQUENCE?

CALQUENCE may cause serious side effects, including:

- **Serious infections** can happen during treatment with CALQUENCE and may lead to death. Your healthcare provider may prescribe certain medicines if you have an increased risk of getting infections. Tell your healthcare provider right away if you have any signs or symptoms of an infection, including fever, chills, or flu-like symptoms.
- **Bleeding problems (hemorrhage)** can happen during treatment with CALQUENCE and can be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you have any signs or symptoms of bleeding, including:
  - blood in your stools or black stools (looks like tar)
  - pink or brown urine
  - unexpected bleeding, or bleeding that is severe or you cannot control
  - vomit blood or vomit that looks like coffee grounds
  - cough up blood or blood clots
  - dizziness
  - weakness
  - confusion
  - changes in your speech
  - headache that lasts a long time
  - bruising or red or purple skin marks
- **Decrease in blood cell counts.** Decreased blood counts (white blood cells, platelets, and red blood cells) are common with CALQUENCE, but can also be severe. Your healthcare provider should do blood tests to check your blood counts regularly during treatment with CALQUENCE.

(continued)

- **Second primary cancers.** New cancers have happened in people during treatment with CALQUENCE, including cancers of the skin or other organs. Your healthcare provider will check you for skin cancers during treatment with CALQUENCE. Use sun protection when you are outside in sunlight.
- **Heart rhythm problems (atrial fibrillation and atrial flutter)** have happened in people treated with CALQUENCE. Tell your healthcare provider if you have any of the following signs or symptoms:
  - fast or irregular heartbeat
  - dizziness
  - feeling faint
  - chest discomfort
  - shortness of breath

The most common side effects of CALQUENCE include:

- headache
- diarrhea
- muscle and joint pain
- upper respiratory tract infection
- bruising

These are not all of the possible side effects of CALQUENCE.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store CALQUENCE?

- Store CALQUENCE at room temperature between 68°F to 77°F (20°C to 25°C).

Keep CALQUENCE and all medicines out of the reach of children.

General information about the safe and effective use of CALQUENCE.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use CALQUENCE for a condition for which it was not prescribed. Do not give CALQUENCE to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for more information about CALQUENCE that is written for health professionals.

What are the ingredients in CALQUENCE?

Active ingredient: acalabrutinib

Inactive ingredients: silicified microcrystalline cellulose, pregelatinized starch, magnesium stearate, and sodium starch glycolate.

Capsule shell contains: gelatin, titanium dioxide, yellow iron oxide, FD&C Blue 2, and black ink.

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US-34063 11/19

Above the Surface

As part of its Speaking Out *video series,* CURE® *spoke with Dr. Steven M. Horwitz on behalf of the Cutaneous Lymphoma Foundation about cutaneous T-cell lymphoma and options for treatment.* By KRISTIE L. KAHL

CONSIDERED A RARE BUT manageable disease, cutaneous T-cell lymphoma (CTCL) is a type of non-Hodgkin lymphoma that affects about 6 per 1 million individuals.

Unlike many other cancer types, CTCL is a cancer of the T lymphocytes, a type of white blood cell, that mainly affects the skin, but also involves the blood, lymph nodes or internal organs.

To better understand the disease and its treatments, *CURE*® spoke with Dr. Steven M. Horwitz of UCI Health on behalf of the Cutaneous Lymphoma Foundation about CTCL and what patients should know about their disease.

Q: *CURE*®: Can you discuss how cutaneous T-cell lymphoma is staged?

A: Dr. Steven M. Horwitz: Cutaneous T-cell lymphoma, sort of by the name, is a lymphoma, a cancer of certain kinds of white blood cells, T cells in this case. In most patients, it starts in the skin, and in many, it's only in the skin. So we do give it a numerical stage based on how much is in the skin. The critical features in that are whether there's a lot of skin involved or just a little bit, and we quantify how much skin is involved based on percentage of skin involvement. Your palm and four fingers (are) about 1% of your body surface area. (We consider) whether the lesions are relatively flat, smooth or a little bit rough, which we call patches and plaques, or whether they're lumpy or what we call tumors, and whether there's any significant disease inside the body.

When you put all that together, we give it a numerical stage, which is sort of descriptive. But I think that tells the doctor whether the treatment can be skin only, or needs to be skin plus medicines that go inside the body, and what kind of treatments are potent enough for the amount of disease you have.

Q: Can you discuss the difference between what's considered aggressive disease and what's indolent disease?

A: For lymphomas, we talk about aggressive and indolent. And what that really means to the doctor is the rate of growth. Lymphomas that tend to grow slowly, we call indolent. It doesn't mean they're not dangerous lymphomas. When they tend to grow quickly, we call (them) aggressive. It doesn't necessarily mean they're dangerous, but different treatments and different treatment strategies lend themselves to that.

For most people with cutaneous T-cell lymphoma, the disease grows at a relatively slow rate. And that means that it grows over many months or years, not days to a month or two. And we would call that an indolent growth rate. But people with more advanced disease, tumors or lumps, or significant disease in the body, are at more risk, or there's more danger from the disease. We can think about those lymphomas as behaving not as a necessarily aggressive growth rate, but more like aggressive in terms of the risk to the person. And then sometimes the treatments we give need to be a little more intense or more reliably active to get good control of that disease relatively quickly. Whereas with a very slow-growing disease, you might lean toward very mild treatments that have as little side effect as possible, knowing that you have a lot of time to slowly get the disease under control.

Q: And similar to that, how does staging play a role in treatment options?

A: The main thing about staging for skin lymphomas is whether the disease is inside the body or not. If there's disease in the blood or lymph nodes, then the way to address the disease has to be with medicines. It could be chemotherapy, it could be immune system therapy, but medicines that treat the inside of the body, as opposed to the majority of people with skin lymphomas where the treatment will be largely directed at the skin — light treatment, topical treatments, things you put on the skin — but no real treatment inside the body. And I think in terms of stage and treatment, that's really the most critical distinction.

Q: How do physicians determine when to change treatment for a patient?

A: This is something that involves a lot of discussion and back and forth and what we call joint decision-making, meaning my goal as a physician is that you are well and healthy and live your full life while I keep the disease under control and minimize the risk to you. And I think most patients are aligned with that. But what happens when the disease is on the skin is there's also visible disease, there are symptoms from the disease, and sometimes the most potent therapies that get the skin looking better and feeling better may limit or take away options for the future or may cause more risk of side effects. Then it's sort of a balance, meaning I want the safest, mildest therapy to keep you well. Many patients also want to look better and feel better as soon as possible, which is totally, really valid. And then how do we negotiate that in terms of what treatments make sense to try? When do we say this is not working well enough, we need to »

add or modify, or when is this clearly the safest treatment? And we need to give it a little longer to see the slow benefit for the long-term gain or the overall safety? And it's a lot of back and forth and discussion with that.

Q: If a disease does progress, what are the best treatment options that we have available right now?

A: It's always hard to make a general statement of what are the best because, again, there are those different dynamics in terms of what our goals of therapy are, the best treatment. Answering in a simplistic way is the one that gets your disease better and doesn't cause any side effects. Or, because we keep these (patients on these) treatments for a long period of time, (choosing a treatment that) doesn't cause any cumulative side effects, to where if it's working, we can keep going. We're more worried about treatments that cause accumulation of side effects or strong immunosuppression, things that could weaken the immune system, put people at risk of infection. So really, the best treatments are those that are effective, but also those that don't accumulate side effects or aren't too harsh on the immune system.

Q: How does advanced systemic therapy play a role in treatment?

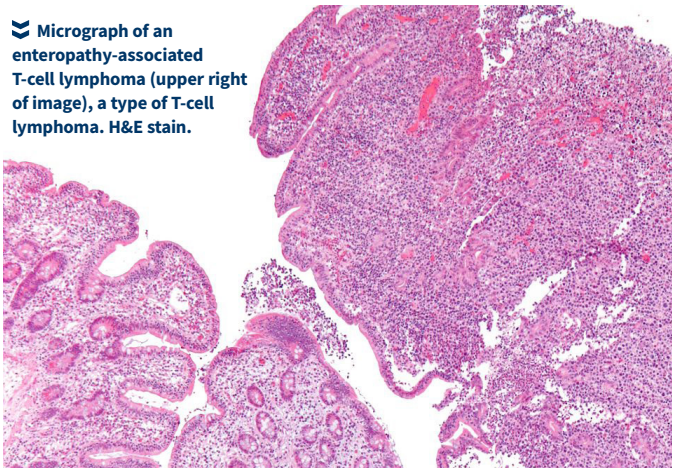
A: We add systemic therapy either when there's disease inside the body or when skin-directed therapies are not adequately controlling it. So that might be adding a mild therapy like a retinoid. There's a medicine called Mekinist (trametinib) that we add frequently, which might boost light therapy, make light treatment or phototherapy to the skin work better, might add a little bit of mild systemic therapy. And there are other medicines that can do the same thing.

When the disease is really progressing at a faster rate inside the body, then we really need more potent treatments that address that. In the past that was primarily chemotherapy. And chemotherapy was often a bad long-term deal for people with cutaneous lymphomas, because while they can work at controlling the lymphoma, there is some accumulation of side effects. And it's very hard to safely be on those treatments for the years and years of life that we're hoping people achieve.

So there are drugs called histone deacetylase inhibitors. … They can work in different ways to control the lymphoma without really suppressing the immune system. More and more, we're having immune-based therapies and in some ways, harnessing or adding to the normal immune system to fight cancer overall, but including cutaneous T-cell lymphoma. That is often a better, safer long-term solution.

There are also antibodies, a drug called mogamulizumab, or Poteligeo, which treats by targeting the immune system to fight the lymphoma cells. It's particularly good in Sezary syndrome. There are some other new treatments being developed along the same lines.

And then other treatments that unlock or unleash the immune system, things that we call T cells, checkpoint inhibitors, treatments like that. There's a drug called (Adcetris



Micrograph of an enteropathy-associated T-cell lymphoma (upper right of image), a type of T-cell lymphoma. H&E stain.

NEPHRON / COMMONS.WIKIMEDIA.ORG

[brentuximab vedotin]), which uses an antibody to target chemotherapy, rather than to the whole body, specifically just to the cancer cells, or mostly to the cancer cells.

So there are a lot of advances in those treatments that, while potent enough to get systemic disease under control, don't really have those significant or strong, limiting side effects that you can't be on them very long. Other things that you'll see in other cancers that are just starting to be understood in cutaneous T-cell lymphoma are some strategies that teach other arms of the immune system, something called macrophages, or CD47. That's a pathway that you can block to try to target the immune system to fight the lymphoma, and then cellular therapy trying to teach your own cells or cells from another person to sort of re-engineer them, what we call chimeric antigen receptor T cells or other forms of genetically engineered cells, to use those cells to fight the lymphoma. Those are in very early-phase clinical trials. But I think a lot of us see that, as we go forward, those may be the more significant breakthroughs in the future.

Q: How does auto stem cell transplantation come into play for a treatment option?

A: So autologous stem cell transplantation is really a way of giving very intensive, very high doses of chemotherapy to try to treat the residual lymphoma, and sometimes leukemia. The side effect of that intensive therapy is that the normal bone marrow, the normal stem cells, would be damaged severely. So you harvest the autologous cells, give the strong chemotherapy, then give those cells back so you can have normal blood counts. What has been learned in past decades is that autologous stem cell transplantation or strong chemotherapy in general can have short-term benefit in controlling cutaneous T-cell lymphomas, but there's almost never long-term benefit. As opposed to some other types of aggressive lymphoma … and the disease usually comes back. We almost never use autologous transplant for cutaneous T-cell lymphoma.

I think our hope is with some of these better immune therapies as we get more therapeutic advances, the need for allogeneic stem cell transplant will be less and less.

Bare Minimum

A meta-analysis found that minimal residual disease positivity after particular treatment for mantle cell lymphoma can predict worse survival benefit. By KRISTIE L. KAHL

MINIMAL RESIDUAL DISEASE (MRD) positivity after induction and consolidation therapy appeared to be associated with worse progression-free and overall survival in patients with mantle cell lymphoma (MCL), according to study findings published in the *Journal of Cancer*.

Patients with advanced MCL tend to be treated with high-dose chemotherapies, chemoimmunotherapies and nonchemotherapeutic agents, such as front-line induction treatment, autologous stem cell transplantation (ASCT) consolidation or Rituxan (rituximab) maintenance after ASCT. Unfortunately, despite some survival benefit, most patients will relapse eventually.

"Also, the toxicities and economic burden from consolidation and maintenance treatment can still be the problems," the researchers said. "Therefore, early assessment of treatment efficacy and response-guided therapy are necessary in MCL management."

MRD refers to a small number of cancer cells that are left in the body after treatment, and can also play a role in determining whether the disease has the potential of coming back and causing a relapse. In recent years, studies have shown that MRD could provide evidence for early response of treatment efficacy.

"Previous studies showed that MRD assessment could predict survival outcomes in MCL," the researchers added. "Also, in some previous clinical trials, surveillance of MRD can monitor response to prior therapy and may inform the need for further consolidation or maintenance therapy in MCL."

However, despite previous trials being conducted in this area, according to the researchers, the sample sizes of each study were typically small. Therefore, the researchers conducted a meta-analysis to further understand the impact of MRD on survival outcomes in newly diagnosed MCL.

Ten articles were included in the quantitative meta-analysis, with all 10 reporting on MRD-related progression-free survival, or the time from treatment to disease progression or worsening, and six reporting on MRD-related overall survival, or the length of time that a patient is still alive from either the date of diagnosis or the start of treatment.

In nine studies, MRD was assessed after the completion of induction treatments, while four studies reported MRD status and the related survival outcomes after ASCT or during maintenance.

To evaluate the impact of post-induction MRD status on progression-free survival, data were extracted from nine studies involving 607 patients, including 246 who were MRD positive and 361 who were MRD negative. For the impact of post-induction MRD status on overall survival, data were extracted from six studies involving 326 patients, including 141 who were MRD positive and 185 who were MRD negative.

Patients who were MRD positive demonstrated shorter progression-free and overall survival compared with patients who were MRD negative. Moreover, the pooled five-year progression-free survival for MRD-positive patients was 42.8%, compared with 68.9% for MRD-negative patients. Similarly, the pooled five-year overall survival rates were 63.6% and 82.3%, respectively.

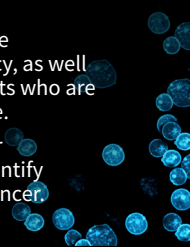
To evaluate post-consolidation MRD status on progression-free survival, data were extracted from four studies involving 489 patients, including 111 who were MRD positive and 378 who were MRD negative. To evaluate post-consolidation MRD status on overall survival, data were extracted from two studies involving 210 patients, including 36 who were MRD positive and 174 who were MRD negative.

Again, positive MRD status was associated with short progression-free and overall survival, compared with those who were MRD negative.

"MRD status after both induction therapy and consolidation therapy showed prognostic value. This may provide information for deciding timing of MRD assessment. On the one hand, post-induction and post-consolidation MRD status assessment could be useful because it has prognostic value and may provide information for further therapy decision-making," the researchers wrote. "On the other hand, as MRD implies the depth of molecular remission, continuous assessment of MRD status can be a useful tool for monitoring early relapse."

What You Need to Know About MRD

- MRD positive means disease was still detected after treatment.
- MRD negative means no disease was detected after treatment.
- Doctors use samples from blood or bone marrow aspiration.
- MRD can measure treatment efficacy, as well as predict patients who are at risk for relapse.
- MRD can monitor remissions or identify early return of cancer.



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Triplet Therapy Improves Progression-Free Survival in Multiple Myeloma

This treatment strategy contributed to better outcomes compared with Velcade and dexamethasone. By DARLENE DOBKOWSKI, M.A.

TREATMENT WITH XPOVIO (selinexor) when added to Velcade (bortezomib) and dexamethasone once per week effectively improved progression-free survival (PFS) in patients with multiple myeloma who previously received up to three lines of therapy, according to findings published in *The Lancet*.

"It should be emphasized that the (Xpovio, Velcade and dexamethasone) regimen, apart from improving progression-free survival and a favorable treatment tolerance profile, is convenient for patients who come to the clinic 35% less often, receive oral and subcutaneous (under the skin) treatment, which improves their comfort," said Dr. Sebastian Grosicki, assistant professor at the Medical University of Silesia in Katowice, Poland, in an interview with *CURE*®.

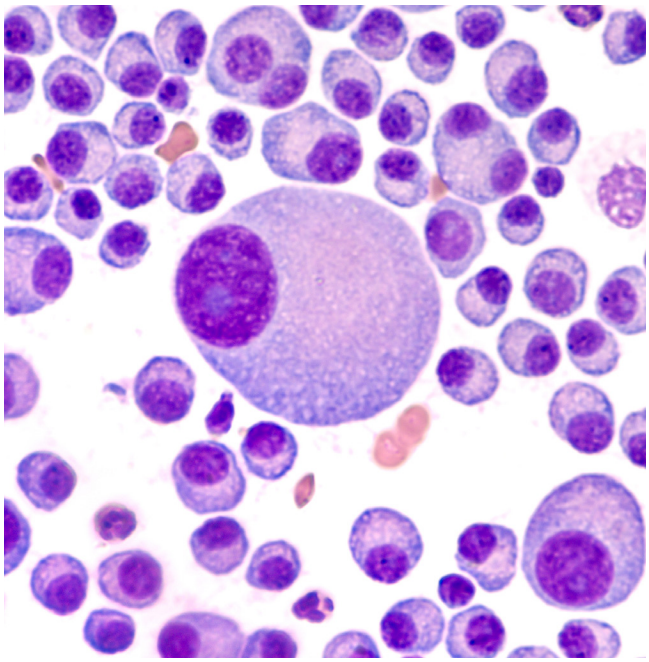
Velcade with low-dose dexamethasone has been the standard therapy for patients with multiple myeloma, although the twice-per-week regimen has been linked with high rates of motor, sensory and autonomic neuropathy (numbness, weakness and pain from nerve damage in hands and feet). Some of these issues can be irreversible, which limits the long-term use of this therapy.

In the phase 3 BOSTON trial, researchers analyzed data from 402 patients with multiple myeloma who were previously treated with up to three lines of therapy including proteasome inhibitors. Patients were randomly assigned treatment with one of two regimens:

- 100 mg of Xpovio once per week, 1.3 mg/m^2 of Velcade once per week and 20 mg of dexamethasone twice per week (195 patients; median age, 66 years; 59% men), or
- 1.3 mg/m^2 of Velcade twice per week for the first 24 weeks then 20 mg of dexamethasone four times per week, for the first 24 weeks then twice per week afterward (207 patients; median age, 67 years; 56% men).

The primary end point of this trial was progression-free survival, defined as the time from the random assignment of a treatment until first disease progression or all-cause death. Patients assigned the Xpovio, Velcade and dexamethasone regimen were followed up for a median of 13.2 months, compared with 16.5 months for patients assigned Velcade and dexamethasone.

Median progression-free survival was significantly longer in the Xpovio, Velcade and dexamethasone group versus the Velcade and dexamethasone group (13.93 months versus 9.46 months).



Multiple myeloma awareness: Bone marrow aspirate cytology of multiple myeloma, a type of bone marrow cancer of malignant plasma cells that is associated with bone pain, bone fractures and anemia.

The grade 3 to 4 side effects that occurred most frequently in patients assigned Xpovio, Velcade and dexamethasone compared with those assigned Velcade and dexamethasone included fatigue (13% versus 1%, respectively), thrombocytopenia (low platelet levels; 39% versus 17%), pneumonia (11% for both groups) and anemia (lack of healthy red blood cells; 16% versus 10%). Peripheral neuropathy grade 2 or above occurred less frequently in the Xpovio, Velcade and dexamethasone group compared with the Velcade and dexamethasone group (21% versus 34%).

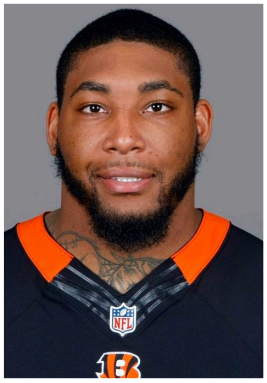
During follow-up, 24% of patients assigned Xpovio, Velcade and dexamethasone died, versus 30% of those assigned Velcade and dexamethasone.

"The results of the study introduce an additional treatment option (Xpovio, Velcade and dexamethasone) that may break resistance to previous treatments," said Grosicki. "We have received a new orally and subcutaneously (Xpovio, Velcade and dexamethasone) weapon against the very insidious enemy of (relapsed/refractory multiple myeloma)."

Program Honors 'Warriors' in Myeloproliferative Neoplasms

The eighth annual MPN Heroes® program, sponsored by CURE® and Incyte, recognized eight individuals. By RYAN MCDONALD

A WIN, OR ACCOMPLISHMENT, is usually attributed to a team of individuals working toward an end goal. Just as it is in most sports, a team effort is needed to score a victory over a cancer diagnosis, former NFL player Devon Still said during the eighth annual MPN Heroes® program, sponsored by *CURE*® and Incyte, in December.



"One thing I understand from sports is that a lot of these victories are a team effort, right? It takes the doctors, it takes the advocates, it takes the researchers, the scientists, it takes the family. Not just the patient, but also the family, because they take on a lot during this battle and, of course, it takes warriors to continue to fight," Still said during his keynote speech. "We're fighting out there for every family who is battling this disease. So we have to come together as a team and put forth our best effort to make sure that this community rises over the challenges that we will face."

In 2015, two months after Still almost died from blood clots in his lungs following back surgery, his daughter, Leah, was diagnosed with a rare pediatric cancer. Still returned to the gridiron wearing Leah's message of hope each game via eye black that read "Leah Strong." Now, through the Still Strong Foundation, Still has partnered with socially conscious organizations to raise more than $2 million to bring awareness to cancer and financially assist families whose children have cancer.

DEVON STILL comforts his daughter, Leah, while she receives treatment for her cancer in 2015.

Still spoke to attendees about why it's important to bring the cancer community together and honor these heroes.

"Going through (cancer), while we're going through a pandemic, is really tough," he said. "Being able to bring families together and let them know that they're not going through it alone, I think it's very important to help and motivate them to continue to fight. Because a lot of times, when we're going through tough battles in our lives, we feel like we're the only ones who are going through it. But when you're able to talk to other people, other families who are going through those same obstacles you are, you're more inclined to continue to fight."

During the MPN Heroes® program, eight individuals — five patient advocates, two oncologists and one caregiver — were awarded for their dedication to patients with myeloproliferative neoplasms (MPNs).

NICK CALLAHAN

ORCHESTRATING OPTIMAL SUPPORT

Nick Callahan has been a best friend and committed caregiver to his significant other, Toula Bonié, since they met in 1991. He said he views his role mostly as a facilitator, doing whatever is needed to help Bonié overcome the challenges of essential thrombocythemia (ET).

"As time has gone on, more and more things have occurred, from dizziness to muscle spasms to extreme itchiness," Bonié said during the event. "Nick didn't even think about what he would do. He just did it."

Callahan will go grocery shopping, cook, run various errands and drive Bonié, who is a violinist, to the backstage door of The Florida Orchestra for her concerts, a perk they lightheartedly refer to as "princess service."

"Becoming (a) caretaker, it's not a conscious approach," he said during the event. "It's just a transition of helping somebody, basically, to minimize whatever pain or suffering they have and to help them get through especially the episodes when they're suffering or in pain."

HIKING FOR MPN AWARENESS

Michele A. Couri has transformed her love of hiking and the outdoors into an awareness and fundraising program »

organization. A full-time obstetrician, Couri originally received a diagnosis of polycythemia vera (PV); however, her condition has since transformed into myelofibrosis (MF).

Couri first became interested in being a patient advocate for MPN when she befriended Bob Rosen, founder of the MPN Research Foundation. When Bob died in 2018, Couri created MPN Peoria to honor his legacy. In two years, the organization has raised $150,000 through two hikes in Illinois, one of which was virtual because of the COVID-19 pandemic. Couri said she was expecting fundraising for 2020's event to be small because of the pandemic, but it surpassed the inaugural event by $30,000.

MICHELE A. COURI

"She has a servant's heart, humble, and a warrior spirit," said Mary Walsh, co-chair of MPN Peoria, during the event. "When she puts her mind to something, she does it. She continues to inspire so many people, not just by telling her story of MPNs, but by who she is."

SUNSHINE AND GOOD HUMOR

Summer Golden has used her sense of humor to impact the lives of thousands of individuals within the MPN community.

An MPN network manager for the Patient Empowerment Network, Golden, who lives with MF, has infused her passion for making people laugh into her work. She helps enhance patient health literacy to enable shared decision-making and provides educational resources that empower patients and caregivers at every step of their cancer journey. When she is not advocating for the MPN community, Golden and her husband, Jeff Bushnell, run the North Park Vaudeville & Candy Shoppe, San Diego's "smallest, sweetest theater" and home to the STARS acting program for people with disabilities.

SUMMER GOLDEN

"Summer has this unique, positive personality, and I think it flows out from her," Bushnell said during the event. "Our story, and what Summer is trying to get across, is you only are given one life to live. And you've got to play the high hand that's dealt to you, (so) make the most of it and not be controlled by this disease."

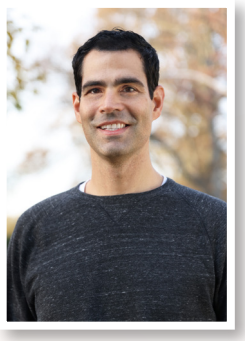
DR. RAMI S. KOMROKJI

REINVIGORATING CARE FOR VETERANS

Dr. Rami S. Komrokji has authored or co-authored more than 200 peer-reviewed manuscripts, 20 book chapters and 300 abstracts on blood cancers. However, Komrokji, who is vice chair of the Malignant Hematology Department and lead clinical investigator for the MDS program at the Moffitt Cancer Center in Tampa, Florida, is known in the MPN community for a different achievement.

While at the University of Cincinnati, he reactivated the Association of VA Hematology/Oncology, serving as president and vice president at various times.

"Honestly, it's very rewarding to take care of those patients," he said during the event. "I'm still excited and enthusiastic to give much more to the patients, to the research community and to the younger people that we are training."



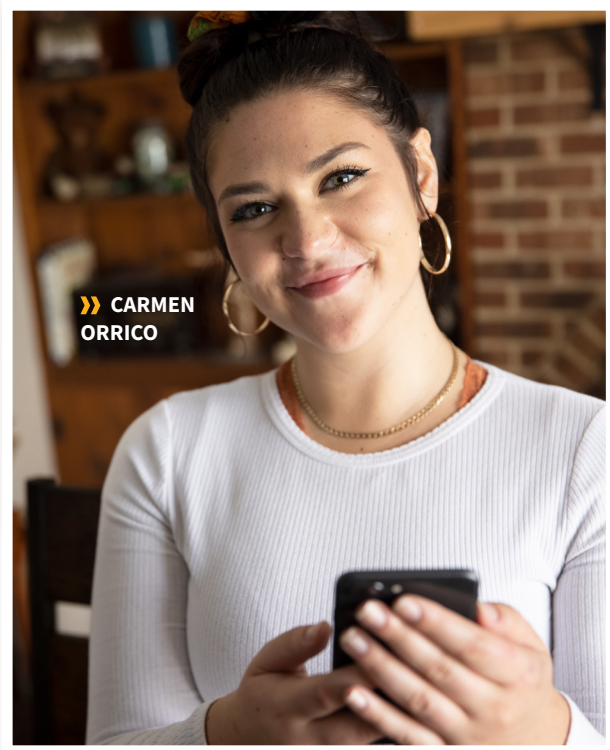
NICK NAPOLITANO

SLOWLY OPENING UP ABOUT MPNS

When a routine physical in 2016 found that Nick Napolitano had PV, he was hesitant to talk about the disease or its symptoms. But after a conversation with his wife, he decided to start eating healthier, work out more and connect with others in the MPN community.

He then shared his story in "The Unknown," a documentary in which he discusses his determination to help others meet the challenges of living with an MPN. In addition to participating in numerous webinars and virtual meetings, Napolitano recently partnered with Patient Power to create and share COVID-19 coping tips for patients with MPNs.

"We're a small community, the MPN community, but we're a strong community and we need each other," he said during the event. "So it's extremely important to share your story. I do whatever I can to create awareness to make sure that people understand, so if it helps one person, that makes me happy."



CARMEN ORRICO

CONNECTING WITH PEERS

Carmen Orrico was diagnosed with ET at the age of 17, which is uncommon, as most cases of the rare condition occur in adults older than 50. When she was first diagnosed, she noticed there was very little information that could help her connect with other young patients.

To bring greater awareness to the condition and share resources that might help others overcome obstacles presented by the condition, Orrico created an Instagram account about ET. Now many young adults around the world share stories and compare notes about managing the condition.

"She's kind of giving a voice to young people who might get brushed aside, letting people know that life can go on, and that you've got to approach it from a healthy perspective, that despite this challenge, you can still try to have a normal life," Carmen's mother, Natalie Catalano, said during the event.

DR. DAVID S. SNYDER

REFLECTING ON AN EXTENSIVE CAREER

Dr. David S. Snyder has helped advance the science of MPNs through research and clinical trials in his more than 40-year career.

Snyder, associate chair in the Department of Hematology & Hematopoietic Cell Transplantation at the City of Hope Comprehensive Cancer Center in Duarte, California, has emphasized education as a cornerstone of patient empowerment for the MPN community. Through patient advocacy forums and one-on-one conversations with patients, Snyder has helped people with MPNs live with hope, strength and courage.

"I'm heading soon toward retirement. And I have sadness, but I also feel gratitude that I've been able to contribute, as I have to build on the work of people who have come before me, as well as what I've shared with my colleagues around the country around the world over 36 years," he said during the event. "I've tried to dedicate myself to our patients, to being the best clinician, the best doctor that I can be for our patients. And I try to bring patients and families along in this journey that we're all traveling together."

PASSION FOR ADVOCACY

Hon. Col. Dr. Samuel Verniero Jr. has spoken with authority for individuals with disabilities because he knows what it's like to live with one. He lives with PV and other medical conditions.

HON. COL. DR. SAMUEL VERNIERO JR.

Verniero has used his public platform and contacts on various boards and commissions to "push really hard" to raise awareness for people with MPNs and other disabilities. He continues to work for change and voice the need for additional MPN research that could improve the lives of patients with MPNs.

"He always uses these things to bring awareness to the MPN community. Even if he's meeting with someone in passing, he never misses an opportunity to share it," Verniero's girlfriend, Lanora Kelley, said during the event. "He's got the kindest, most compassionate heart. He's constantly doing just every little thing to help another person."

A TEAM OF HEROES

Erik Lohrmann, vice president of oncology at CURE Media Group, thanked those who attended the virtual event.

"MJH Life Sciences™ and CURE® magazine, with support from Incyte, are honored to recognize these eight individuals who have dedicated their lives and careers to improving the care for MPN patients," said Lohrmann during the event. "To Incyte, on behalf of MJH Life Sciences™, *CURE*® and our heroes, thank you for making tonight possible. Lastly, to our heroes, you've each gone above and beyond in your own unique way and are truly the embodiment of what the heroes award represents."

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Managing Cancer Scares During a Pandemic

Navigating the scary path of a cancer caregiver possibly becoming the patient with cancer. By SHIRA ZWEBNER

SHIRA ZWEBNER, a native New Yorker, is a communications consultant and writer living with her husband and three children in Jerusalem. In 2017 she received a diagnosis of diffuse large B-cell lymphoma, and is fighting her cancer battle and blogging about the journey at hipstermomblog.com.

I HAVE BEEN ANNOYING MY husband about seeing a dermatologist for years. When he entered his 40s, I started subtly nagging. Each time I went to see the dermatologist, I would gently suggest that he schedule an appointment for a routine scan, too, just to make sure everything was OK.

To my untrained eye, he didn't have anything that looked like it needed to be checked out, but I believe in the "better safe than sorry" philosophy of life. With a grandmother who died from melanoma, I was paranoid about my skin. Yet my husband preferred to just let things be, and so for years, he managed to avoid the dermatologist.

When I received a diagnosis of stage 4 diffuse large B-cell lymphoma, I stopped the nagging and surrendered myself to the care of my hematology-oncologist and my husband. For months, my husband was my full-time caregiver, shuttling me to and from treatment appointments and weekly blood tests, scheduling scans and filling prescriptions. He physically hauled me off the bathroom floor when I collapsed after violent vomiting fits and stood outside my shower door with a towel, ready to quickly remove the waterproof cuff that we used to keep my PICC line dry and sterile.

He kept the home fires burning with our three small children while holding down a full-time job, waking up early to make school lunches and staying up late to review homework. He listened to my fears, held me when I cried and made sure I stayed hydrated, medicated and sane. I would not have made it through treatment without him.

When treatment ended and recovery began, I started nagging him again. I didn't stop at the dermatologist; I wanted him to have a colonoscopy and more bloodwork. His health became my top priority. I needed him to be healthy and not just because I needed him in his capacity as a caregiver, but because I needed to know that our children would have at least one healthy parent. I learned that life could throw us curveballs and when they did, they were usually thrown at me, so he needed to be the stable one in their life.

So when I saw my dermatologist over the summer, I decided to stop asking my husband to make the appointment and I made one for him. As with many dermatologists, the earliest appointment wasn't for three months, but I booked the time slot anyway and sent him a calendar invite. We were both convinced the appointment would be routine, so I stayed home when he went for his full body scan.

Distractedly, I sent him a text that morning to check in and he replied, "She found something." Shock, then disbelief, followed. When he finally called me, he said she saw something on his back that she wanted to be removed ASAP. She said it was probably nothing, but well, we all know that "probably nothing" always has the potential to turn into something. Dazed, my husband managed to pick up a canceled appointment with a plastic surgeon and he scheduled the mole removal for the following morning. It was an appointment I didn't miss, and suddenly our roles reversed and I became the caregiver.

If I'm being honest, I suck as a caregiver. For less than 24 hours of post-mole removal, I catered to his every need. I fluffed his pillow and prepared his meals, I let him recover in bed and made sure the children were taken care of. I bought him a new comic book to lift his spirits and some chocolate to feed the fear. But I also made him walk the dog and after two days off work, I told him it was time to get back to the office.

I couldn't handle seeing him lying in bed, his fragility a stark reminder that I have no control over which one of us gets sick. As much as I've been working on keeping him healthy and strong, at the end of the day, I have little choice or say in the matter.

For five weeks, we skirted around the cloud that was hanging over our heads, waiting for the pathology report. We know better than to tell ourselves that everything will be OK until we know it's OK. So we focused our energies elsewhere, trying to keep routine to our day while keeping our fears to ourselves. Once again, we kept our children in the dark as we waited for the results.

This morning, as we entered the first full day of another COVID-19-related national lockdown, we got the call that the pathology report indicated that the mole was benign. I let out the breath I've been holding for five months, thanked God for the good news and started nagging about the colonoscopy next.

ILLUSTRATION BY RAY PELESKO

We are helping to move mountains for myeloma patients

Moving Mountains for Multiple Myeloma, (MM4MM), is an award-winning collaboration between CURE Media Group and the Multiple Myeloma Research Foundation (MMRF) which raises funds and awareness for myeloma research.

Since its inception in 2016, Moving Mountains for Multiple Myeloma teams have climbed Mt. Kilimanjaro, hiked the Grand Canyon, summited Mount Fuji, trekked the Inca Trail to Machu Picchu, reached Everest Base Camp and conquered Iceland's many landscapes. Our team members have raised over $2.9 million, 100% of which goes directly to the MMRF, which spearheads and funds critical myeloma research. These amazing journeys are captured via blogs, social media posts, and video.

Due to COVID-19 the 2020 program has shifted - all 2020 teams will continue fundraising and training this year and will hike in early 2021.

Patients, caregivers, myeloma loved ones, and others impacted directly by multiple myeloma will take on the Alaskan Kenai Peninsula, summit Mount Washington, explore the terrain of Greenland, and more! They will raise funds for multiple myeloma research and demonstrate that the advancements being made in recent years, led by the MMRF, are helping patients live longer with a higher quality of life than ever before.

To learn more and join a MM4MM team visit:
MovingMountainsForMultipleMyeloma.com

To learn more about the MMRF, visit **TheMMRF.org**

LEARN MORE ABOUT OUR CLIMBS!

2020 TREKS IN 2021!

Mount Washington Hike
July 9-12, 2021

Greenland Trek
To be determined

Alaskan Kenai Peninsula Trek
June 20-26, 2021

Kilimanjaro Trek
March 6-16, 2021

Machu Picchu Trek
May 1-11, 2021

New 2021 hikes & dates coming soon!
Email **teammanager@themmrf.org** to get on our waitlist!

MOVING MOUNTAINS for MULTIPLE MYELOMA

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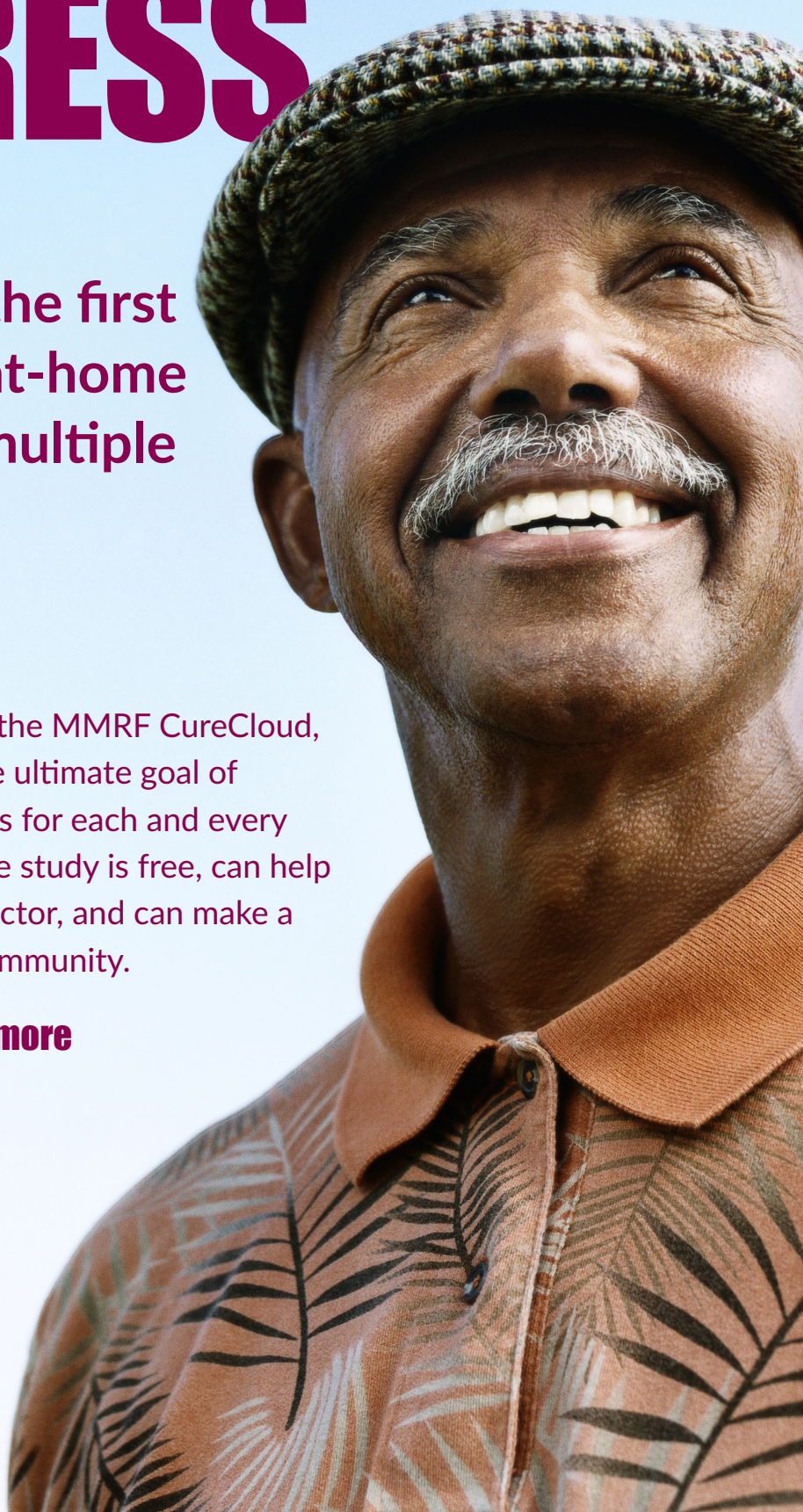
EXPECT PROGRESS

Introducing the MMRF CureCloud®, the first research study with at-home genomic testing for multiple myeloma patients.



Our groundbreaking research study, the MMRF CureCloud, will help accelerate research with the ultimate goal of identifying smarter treatment options for each and every multiple myeloma patient. Joining the study is free, can help inform your discussions with your doctor, and can make a difference for the entire myeloma community.

Visit MMRFCureCloud.org to learn more

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