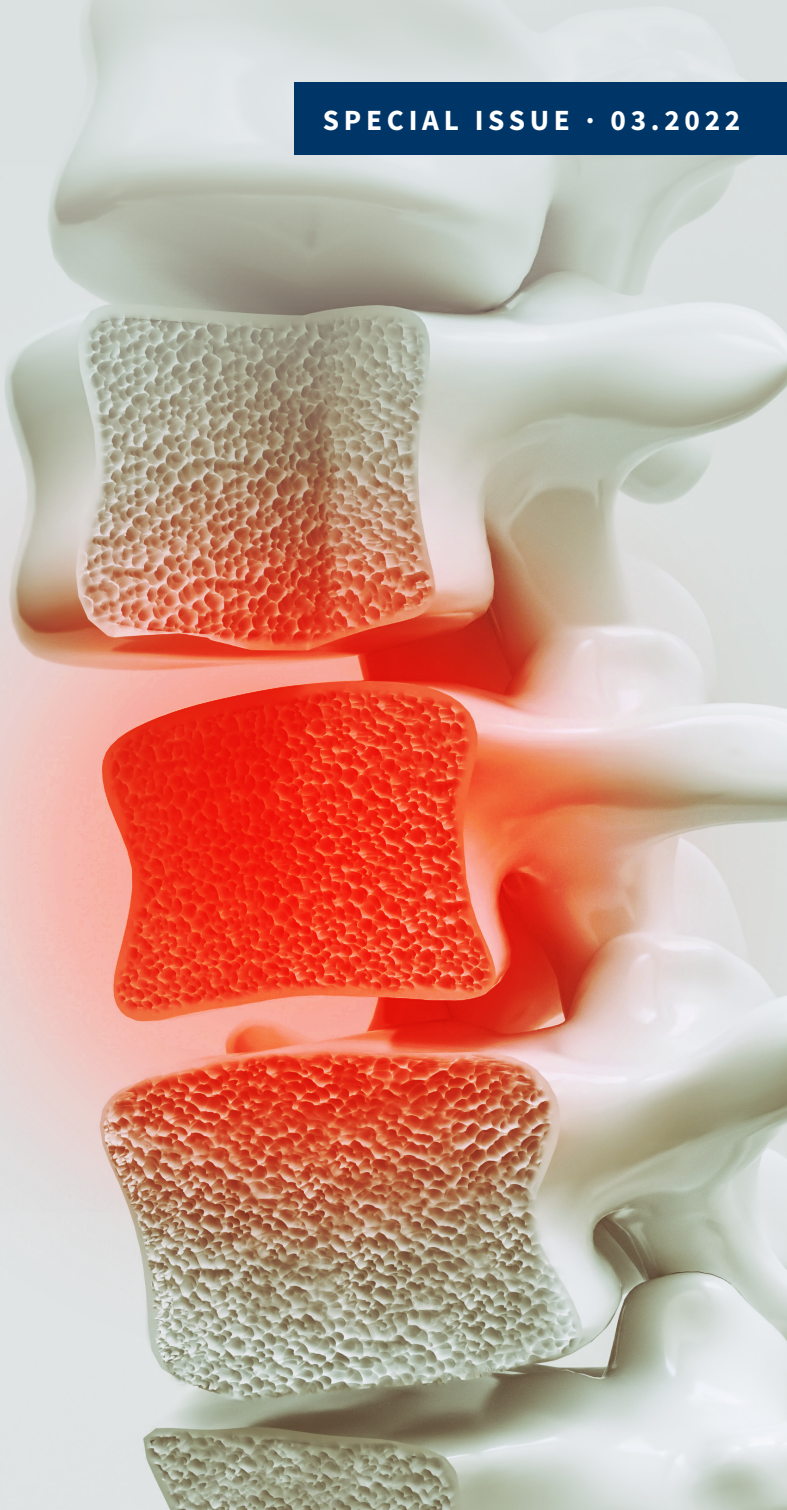
FOR PATIENTS, SURVIVORS & THEIR CAREGIVERS

MULTIPLE MYELOMA
cure® 20TH anniversary
Cancer Updates, Research & Education®

SPECIAL ISSUE · 03.2022

TREATING BONE PAIN IN MULTIPLE MYELOMA

PATIENTS WITH MULTIPLE MYELOMA OFTEN EXPERIENCE BONE PAIN THAT MAY AFFECT THEIR DAILY LIFE, SO WHAT IS THE SOLUTION?



ALSO IN THIS ISSUE

curetoday.com

What is DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj)?

DARZALEX *FASPRO*® is a prescription medicine used to treat adult patients with multiple myeloma:

- in combination with the medicines bortezomib, melphalan, and prednisone in people with newly diagnosed multiple myeloma who cannot receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant)
- in combination with the medicines lenalidomide and dexamethasone in people with newly diagnosed multiple myeloma who cannot receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant) and in people whose multiple myeloma has come back or did not respond to treatment who have received at least one prior medicine to treat multiple myeloma
- in combination with the medicines bortezomib, thalidomide, and dexamethasone in newly diagnosed people who are eligible to receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant)
- in combination with the medicines pomalidomide and dexamethasone in people who have received at least one prior medicine, including lenalidomide and a proteasome inhibitor, to treat multiple myeloma
- in combination with the medicines bortezomib and dexamethasone in people who have received at least one prior medicine to treat multiple myeloma
- alone in people who have received at least three prior medicines, including a proteasome inhibitor and an immunomodulatory agent, **or** did not respond to a proteasome inhibitor and an immunomodulatory agent

It is not known if DARZALEX *FASPRO*® is safe and effective in children.

IMPORTANT SAFETY INFORMATION

Do not receive DARZALEX *FASPRO*® if you have a history of a severe allergic reaction to daratumumab, hyaluronidase, or any of the ingredients in DARZALEX *FASPRO*®. See below for a complete list of ingredients in DARZALEX *FASPRO*®.

Before you receive DARZALEX *FASPRO*®, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of breathing problems
- have had shingles (herpes zoster)
- have ever had or might now have a hepatitis B infection as DARZALEX *FASPRO*® could cause hepatitis B virus to become active again. Your healthcare provider will check you for signs of this infection before, during, and for some time after treatment with DARZALEX *FASPRO*®. Tell your healthcare provider right away if you get worsening tiredness or yellowing of your skin or white part of your eyes.
- are pregnant or plan to become pregnant. DARZALEX *FASPRO*® may harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with DARZALEX *FASPRO*®.
  - Females who are able to become pregnant should use an effective method of birth control (contraception) during treatment and for 3 months after your last dose of DARZALEX *FASPRO*®. Talk to your healthcare provider about birth control methods that you can use during this time.
  - Before starting DARZALEX *FASPRO*® in combination with lenalidomide, thalidomide, or pomalidomide, females and males must agree to the instructions in the lenalidomide, thalidomide, or pomalidomide REMS program.
    - The lenalidomide, thalidomide, and pomalidomide REMS have more information about effective methods of birth control, pregnancy testing, and blood donation for females who can become pregnant.
    - For males who have female partners who can become pregnant, there is information in the lenalidomide, thalidomide, and pomalidomide REMS about sperm donation and how lenalidomide, thalidomide, and pomalidomide can pass into human semen.
- are breastfeeding or plan to breastfeed. It is not known if DARZALEX *FASPRO*® passes into your breast milk. You should not breastfeed during treatment with DARZALEX *FASPRO*®. Talk to your healthcare provider about the best way to feed your baby during treatment with DARZALEX *FASPRO*®.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

- DARZALEX *FASPRO*® will be given to you by your healthcare provider as an injection under the skin, in the stomach area (abdomen).

BE HEARD IN THE FACE OF A MULTIPLE MYELOMA DIAGNOSIS OR A RELAPSE.

Find your voice and learn about your options. Ask your doctor about DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) and if one of its regimens may be a treatment approach for you.

DARZALEX *FASPRO*® is given in **3 to 5 minutes*** as an injection under the skin.
*This refers to the injection administration time and does not account for all aspects of treatment.

It is not chemotherapy. **It's an immunotherapy** that works with your immune system to fight multiple myeloma.

Daratumumab attaches itself to the **CD38 protein** on the surface of multiple myeloma cells, as well as on certain other types of cells, such as red blood cells. Daratumumab **directly kills multiple myeloma cells** and/or allows your immune system to identify and destroy them. Because of the way daratumumab works, it may also affect normal cells.

DARZALEX *FASPRO*® may cause serious reactions, including: serious allergic reactions and other severe injection-related reactions, injection site reactions, decreases in blood cell counts, and changes in blood tests. See Important Safety Information below.

Lift your voice against multiple myeloma—prepare for your next doctor visit at **MyVoiceDarzalexFaspro.com**

DARZALEX *Faspro*®
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

BOLDLY YOU

- DARZALEX *FASPRO*® is injected over 3 to 5 minutes.
- Your healthcare provider will decide the time between doses as well as how many treatments you will receive.
- Your healthcare provider will give you medicines before each dose of DARZALEX *FASPRO*® and after each dose of DARZALEX *FASPRO*® to help reduce the risk of serious allergic reactions and other reactions due to release of certain substances by your body (systemic).

If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

DARZALEX *FASPRO*® may cause serious reactions, including:

- **Serious allergic reactions and other severe injection-related reactions.** Serious allergic reactions and reactions due to release of certain substances by your body (systemic) that can lead to death can happen with DARZALEX *FASPRO*®. Tell your healthcare provider or get medical help right away if you get any of these symptoms during or after an injection of DARZALEX *FASPRO*®.
  - shortness of breath or trouble breathing
  - dizziness or lightheadedness (hypotension)
  - cough
  - wheezing
  - heart beating faster than usual
  - low oxygen in the blood (hypoxia)
  - throat tightness
  - runny or stuffy nose
  - headache
  - itching
  - high blood pressure
  - nausea
  - vomiting
  - chills
  - fever
  - chest pain
- **Injection site reactions.** Skin reactions at or near the injection site (local), including injection site reactions, can happen with DARZALEX *FASPRO*®. Symptoms at the site of injection may include itching, swelling, bruising, pain, rash, bleeding, or redness of the skin. These reactions sometimes happen more than 24 hours after an injection of DARZALEX *FASPRO*®.
- **Decreases in blood cell counts.** DARZALEX *FASPRO*® can decrease white blood cell counts, which help fight infections, and blood cells called platelets, which help to clot blood. Your healthcare provider will check your blood cell counts during treatment with DARZALEX *FASPRO*®. Tell your healthcare provider if you develop fever or have signs of bruising or bleeding.
- **Changes in blood tests.** DARZALEX *FASPRO*® can affect the results of blood tests to match your blood type. These changes can last for up to 6 months after your final dose of DARZALEX *FASPRO*®. Your healthcare provider will do blood tests to match your blood type before you start treatment with DARZALEX *FASPRO*®. **Tell all of your healthcare providers that you are being treated with DARZALEX *FASPRO*® before receiving blood transfusions.**

The most common side effects of DARZALEX *FASPRO*® when used alone include cold-like symptoms (upper respiratory infection).

The most common side effects of DARZALEX *FASPRO*® used in combination therapy include:

- tiredness
- nausea
- diarrhea
- shortness of breath
- trouble sleeping
- fever
- cough
- muscle spasms
- back pain
- vomiting
- cold-like symptoms (upper-respiratory infection)
- nerve damage causing tingling, numbness, or pain
- constipation
- lung infection (pneumonia)
- swollen hands, ankles, or feet

These are not all the possible side effects of DARZALEX *FASPRO*®. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of DARZALEX *FASPRO*®

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your healthcare provider or pharmacist for information about DARZALEX *FASPRO*® that is written for health professionals.

Active ingredient: daratumumab and hyaluronidase-fihj
Inactive ingredients: L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 20, sorbitol, water for injection

Please see Brief Summary of the Product Information on the adjacent page.

cp-143282v5

Janssen Oncology

PATIENT INFORMATION
DARZALEX (Dar'-zah-lex) FASPRO® (Fas-pro)
(daratumumab and hyaluronidase-fihj)
injection, for subcutaneous use

DARZALEX FASPRO may be used with other medicines called lenalidomide, thalidomide or pomalidomide. You should also read **the Medication Guide that comes with lenalidomide, thalidomide or pomalidomide if you use DARZALEX FASPRO with these medicines**.

What is DARZALEX FASPRO?
DARZALEX FASPRO is a prescription medicine used to treat adult patients with multiple myeloma:

- in combination with the medicines bortezomib, melphalan and prednisone, in people with newly diagnosed multiple myeloma who cannot receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant).
- in combination with the medicines lenalidomide and dexamethasone in people with newly diagnosed multiple myeloma who cannot receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant) and in people whose multiple myeloma has come back or did not respond to treatment, who have received at least one prior medicine to treat multiple myeloma.
- in combination with the medicines bortezomib, thalidomide, and dexamethasone in newly diagnosed people who are eligible to receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant).
- in combination with the medicines bortezomib and dexamethasone in people who have received at least one prior medicine to treat multiple myeloma.
- in combination with the medicines pomalidomide and dexamethasone in people who have received at least one prior medicine including lenalidomide and a proteasome inhibitor to treat multiple myeloma.
- alone in people who have received at least three prior medicines, including a proteasome inhibitor and an immunomodulatory agent, **or** did not respond to a proteasome inhibitor and an immunomodulatory agent.

DARZALEX FASPRO is a prescription medicine also used in combination with the medicines bortezomib, cyclophosphamide and dexamethasone in patients with newly diagnosed light chain (AL) amyloidosis.
It is not known if DARZALEX FASPRO is safe and effective in children.

Do not receive DARZALEX FASPRO if you have a history of a severe allergic reaction to daratumumab, hyaluronidase or any of the ingredients in DARZALEX FASPRO. See the end of this leaflet for a complete list of ingredients in DARZALEX FASPRO.

Before you receive DARZALEX FASPRO, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of breathing problems
- have had shingles (herpes zoster)
- have ever had or might now have a hepatitis B infection as DARZALEX FASPRO could cause hepatitis B virus to become active again. Your healthcare provider will check you for signs of this infection before, during and for some time after treatment with DARZALEX FASPRO. Tell your healthcare provider right away if you get worsening tiredness or yellowing of your skin or white part of your eyes.
- are pregnant or plan to become pregnant. DARZALEX FASPRO may harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with DARZALEX FASPRO.
  - Females who are able to become pregnant should use an effective method of birth control (contraception) during treatment and for 3 months after your last dose of DARZALEX FASPRO. Talk to your healthcare provider about birth control methods that you can use during this time.
  - Before starting DARZALEX FASPRO in combination with lenalidomide, thalidomide or pomalidomide, females and males must agree to the instructions in the lenalidomide, thalidomide or pomalidomide REMS program.
    - The lenalidomide, thalidomide and pomalidomide REMS have more information about effective methods of birth control, pregnancy testing, and blood donation for females who can become pregnant.
    - For males who have female partners who can become pregnant, there is information in the lenalidomide, thalidomide and pomalidomide REMS about sperm donation and how lenalidomide, thalidomide and pomalidomide can pass into human semen.
- are breastfeeding or plan to breastfeed. It is not known if DARZALEX FASPRO passes into your breast milk. You should not breastfeed during treatment with DARZALEX FASPRO. Talk to your healthcare provider about the best way to feed your baby during treatment with DARZALEX FASPRO.

Before you receive DARZALEX FASPRO for light chain (AL) amyloidosis, tell your healthcare provider if you have a history of heart problems. DARZALEX FASPRO should not be used in light chain (AL) amyloidosis patients with highly advanced heart disease outside of clinical trials.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive DARZALEX FASPRO?

- DARZALEX FASPRO may be given alone or together with other medicines used to treat multiple myeloma.
- DARZALEX FASPRO will be given to you by your healthcare provider as an injection under the skin, in the stomach area (abdomen).
- DARZALEX FASPRO is injected over 3 to 5 minutes.
- Your healthcare provider will decide the time between doses as well as how many treatments you will receive.
- Your healthcare provider will give you medicines before each dose of DARZALEX FASPRO and after each dose of DARZALEX FASPRO to help reduce the risk of serious allergic reactions and other reactions due to release of certain substances by your body (systemic).

If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of DARZALEX FASPRO?

DARZALEX FASPRO may cause serious reactions, including:

- **Serious allergic reactions and other severe injection-related reactions.** Serious allergic reactions and reactions due to release of certain substances by your body (systemic) that can lead to death, can happen with DARZALEX FASPRO. Tell your healthcare provider or get medical help right away if you get any of these symptoms during or after an injection of DARZALEX FASPRO.
  - shortness of breath or trouble breathing
  - dizziness or lightheadedness (hypotension)
  - cough
  - wheezing
  - heart beating faster than usual
  - low oxygen in the blood (hypoxia)
  - throat tightness
  - runny or stuffy nose
  - headache
  - itching
  - high blood pressure
  - nausea
  - vomiting
  - chills
  - fever
  - chest pain
- **Injection site reactions.** Skin reactions at or near the injection site (local), including injection site reactions, can happen with DARZALEX FASPRO. Symptoms at the site of injection may include itching, swelling, bruising, pain, rash, bleeding, or redness of the skin. These reactions sometimes happen more than 24 hours after an injection of DARZALEX FASPRO.
- **Heart problems in people with light chain (AL) amyloidosis**. Heart problems, in some cases fatal, have occurred. Your healthcare provider will monitor you closely during treatment with DARZALEX FASPRO. Call your healthcare provider right away if you get any of the following symptoms: chest pain, feeling faint, swollen legs, shortness of breath, or abnormal heart rhythm.
- **Decreases in blood cell counts.** DARZALEX FASPRO can decrease white blood cell counts which help fight infections and blood cells called platelets which help to clot blood. Your healthcare provider will check your blood cell counts during treatment with DARZALEX FASPRO. Tell your healthcare provider if you develop fever or have signs of bruising or bleeding.
- **Changes in blood tests.** DARZALEX FASPRO can affect the results of blood tests to match your blood type. These changes can last for up to 6 months after your final dose of DARZALEX FASPRO. Your healthcare provider will do blood tests to match your blood type before you start treatment with DARZALEX FASPRO. **Tell all of your healthcare providers that you are being treated with DARZALEX FASPRO before receiving blood transfusions.**

The most common side effects of DARZALEX FASPRO when used alone include cold-like symptoms (upper respiratory infection).

The most common side effects of DARZALEX FASPRO used in combination therapy include:

- tiredness
- nausea
- diarrhea
- shortness of breath
- trouble sleeping
- fever
- cough
- muscle spasms
- back pain
- vomiting
- cold-like symptoms (upper-respiratory infection)
- nerve damage causing tingling, numbness or pain
- constipation
- lung infection (pneumonia)
- swollen hands, ankles, or feet

These are not all the possible side effects of DARZALEX FASPRO.

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

General information about the safe and effective use of DARZALEX FASPRO.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about DARZALEX FASPRO that is written for health professionals.

What are the ingredients in DARZALEX FASPRO?

Active ingredient: daratumumab and hyaluronidase-fihj

Inactive ingredients: L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 20, sorbitol, and water for injection.

Manufactured by: Janssen Biotech, Inc., Horsham, PA 19044 U.S. License Number 1864
For more information, call 1-800-526-7736 or go to www.DARZALEXFASPRO.com.

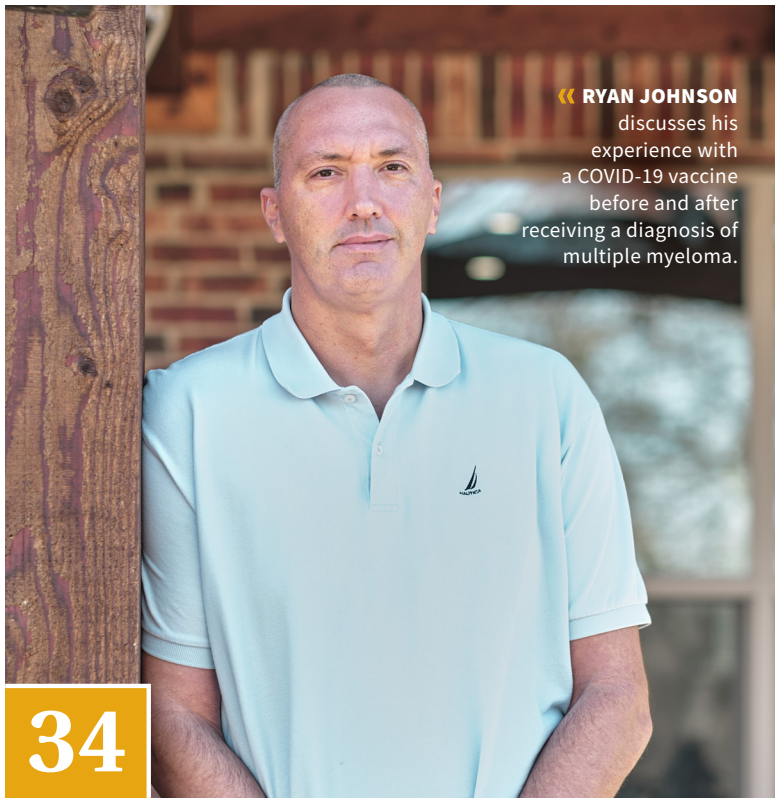
This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 7/2021
cp-145255v4

cure® 20TH anniversary Contents

MULTIPLE MYELOMA SPECIAL ISSUE · 03.22

28

» **JOAN RODRIGUEZ** recalls how finding a new oncologist that listened to her concerns during treatment was intimidating.



34

« **RYAN JOHNSON** discusses his experience with a COVID-19 vaccine before and after receiving a diagnosis of multiple myeloma.

COVER IMAGE: CREVIS / STOCK.ADOBE.COM ADAPTED BY GWEN SALAS; TOP: RYAN JOHNSON BY JARED REY HERNANDEZ; BOTTOM: PHOTO PROVIDED BY JOAN RODRIGUEZ

KENNY CAPPS found relief in exercise when experiencing bone pain.

22

16

« IN THIS ISSUE: ***Patient Spotlight:*** **A look at a patient who found confidence in fashion.**

TOP: KENNY CAPPS BY CARRIE TURNER; BOTTOM: PHOTO PROVIDED BY DONNA MCNUTT

publisher's note

Taking It One Day — *and One Outfit* — at a Time

PATIENTS WITH MULTIPLE MYELOMA often experience bone pain because the disease weakens the bones, making them more fragile. It can be difficult for patients to go about their daily life with this type of pain, so what can help?

During the past 15 years, new treatments have come to the rescue, including additional drug regimens and an increased focus on exercise to keep the body moving and reduce pain. In this special issue of *CURE*®, two patients with multiple myeloma share their stories on how the disease affected their bone health and how they were able to overcome it. Experts also discuss why patients experience bone pain and how they can find relief.

> "It can be difficult for patients to go about their daily life with this type of pain, so what can help?"

CURE® also talks to Donna McNutt, a cancer fashionista who is "fighting cancer one outfit at a time." McNutt finds motivation and confidence in getting dressed every day, and she uses the power of Instagram to share that confidence with others on the same journey.

Also in this issue, two experts weigh in on the advancements that have been made for the treatment of multiple myeloma in the past two decades and where they think the field is headed in the next 20 years.

As always, we hope you find our stories inspirational and informative. Thank you for reading.

MIKE HENNESSY JR.
President and CEO
MJH LIFE SCIENCES®

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cure®

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CURE® (ISSN 1534-7664, USPS 022-616) is published quarterly for cancer patients, survivors and caregivers by CURE Media Group, LLC, Inc., 2 Clarke Drive, Suite 100, Cranbury, NJ 08512. Periodicals postage paid at Princeton, NJ and additional mailing offices. POSTMASTER: Send address changes to *CURE*®, P.O. Box 606, Cranbury, NJ 08512.

Some Immunity Is Better Than None Against COVID-19

THE COVID-19 VACCINES HAVE been one of the most talked about topics in recent years. It's a moving target, with lots of information based on studies of the general population. So it is important for patients with multiple myeloma to understand what some of the uncertainties mean for them. In this special issue of *CURE®*, we learn more about how patients with multiple myeloma are responding to the COVID-19 vaccines and why their immune system's response might not be as great as those without cancer.

> "This is an important issue for patients with multiple myeloma to be aware of and stay educated on."

Many patients with multiple myeloma are immunosuppressed because of faulty immunoglobulin production. This affects both cellular (specialized immune cells that recognize foreign antigens) and humoral (antibody-based) immunity, causing a higher risk of bacterial infections and viral infections such as COVID-19.

One way to fight the risk of contracting an infection such as COVID-19 is to receive a vaccine, but is it as effective in patients with multiple myeloma?

Some patients may not make the same amount and quality of antibodies as people who don't have cancer. But there is a wide spectrum of how immunosuppressed patients are and how they respond to a vaccine.

At this point we don't know who will fully respond to the vaccine and who won't. Many things can influence a patient's response, such as their treatments or whether they have a higher tumor burden. We recommend these patients get vaccinated, first checking with their doctor about when the best time to do so is, depending on their treatment cycle.

As the omicron variant spread, we learned that although it is more transmissible, it is not as virulent. This means all of us are more susceptible to the variant and may have to take more precautions to protect ourselves against it, but if infected we are less likely to have a severe case of COVID-19.

We recommend that patients with multiple myeloma get the standard vaccines and boosters for COVID-19. Remember, even if you don't get full immunity, some immunity is better than none.

DEBU TRIPATHY, M.D.
EDITOR-IN-CHIEF
Professor of Medicine
Chair, Department of Breast Medical Oncology
The University of Texas MD Anderson Cancer Center

TREATMENT

3-Drug Combination Demonstrates Potential for Older Patients

Darzalex plus Revlimid and dexamethasone may be the preferred option to treat older patients who are ineligible for stem cell transplant.

By COLLEEN MORETTI

COMBINING DARZALEX (daratumumab) with Revlimid (lenalidomide) and dexamethasone may improve survival with no safety concerns in patients newly diagnosed with myeloma who are ineligible for stem cell transplant.

"(Although) there are treatment options for these patients right now, given the incurable nature of multiple myeloma, improvements in therapies that will provide for longer duration of response (represent) an ongoing need," Dr. Shaji K. Kumar, one of the study's authors and a professor of medicine at Mayo Clinic in Rochester, Minnesota, told *CURE*®. "This particular regimen provides one of the longest progression-free survival (rates) for patients who are not eligible to undergo an autologous stem cell transplantation."

Patients included in this study, which was published in *Lancet Oncology*, had received new diagnoses of multiple myeloma and were ineligible for high-dose chemotherapy with autologous stem cell transplantation because of age or comorbidities.

Researchers evaluated progression-free survival (time during and after treatment when the patient lives without disease progression) and overall survival (time from receiving a diagnosis or when the treatment started when patients are alive) in 737 patients (median age, 73 years). The Darzalex group (368 patients) received a 28-day cycle of Darzalex plus oral Revlimid and oral dexamethasone. And those in the control group (369 patients) received Revlimid and dexamethasone orally.

At the median follow-up of 56.2 months, median progression-free survival was not reached in the Darzalex group, and was 34.4 months in the control group. Median overall survival was not reached in either group. Kumar explained that when progression-free survival and overall survival are not reached, it is a good thing and highlights a longer survival.

"This is very important, as the overall survival end point remains the gold standard for demonstrating superiority of a treatment approach in multiple myeloma," he said.

The most common side effects that occurred in more than 15% of patients in the Darzalex or control groups included neutropenia (54% versus 37%, respectively), pneumonia (19% versus 11%), anemia (17% versus 22%) and lymphopenia (16% versus 11%). Serious side effects occurred in 77% of patients receiving Darzalex and 70% of those assigned to the control regimen. Treatment-related deaths occurred in 4% of patients in the Darzalex group and 3% of patients in the control group.

These results suggest that Darzalex plus Revlimid and dexamethasone may be an ideal regimen for initial therapy in older patients, Kumar added.

"These results should place this three-drug regimen as a preferred option for patients with newly diagnosed multiple myeloma who cannot undergo an autologous stem cell transplantation and are able to tolerate a three-drug combination. For those patients who cannot tolerate a three-drug regimen, the results with the (Revlimid) and dexamethasone combination suggest that it is also a feasible approach," he concluded.

CAR-T CELL THERAPY

CAR-T Cell Therapy May Have 'Big Future' in Relapsed/Refractory Disease

Durable and deep responses occurred after use of a particular CAR-T cell therapy.

By COLLEEN MORETTI

CARVYKTI (CILTACABTAGENE AUTOLEUCEL), a chimeric antigen receptor T (CAR-T) cell therapy, has induced early, durable responses and manageable side effects in patients with relapsed/refractory multiple myeloma who were previously heavily treated. The results led to an approval by the Food and Drug Administration (FDA) on February 28, 2022, making Carvytki the second CAR-T cell therapy available for this patient population.

The phase 1/2b study included 97 patients (58.8% male; median age, 61 years) who had at least three prior lines of therapy or were refractory to a proteasome inhibitor and immunomodulatory drug. Dr. Thomas G. Martin, lead author on the study and associate director of the myeloma program at the University of California, San Francisco, said in an interview with *CURE®* that most patients in this study had six prior lines of therapy and became refractory, "which is where we get into trouble." The patients had exhausted all other treatment options, so to have another option was important for this population.

In the study, patients received a single Carvykti infusion five to seven days after chemotherapy.

Martin explained that CAR-T cell therapy is an immunotherapy where T cells are taken from the patients and, using gene therapy, are trained to be "professional myeloma killers," by now targeting a protein, BCMA, on the outside of the cell surface. This is one of the first studies using BCMA-targeted CAR-T cells for these patients, he said.

"It's the first step in what's hopefully going to be a big future for these CAR-T cells in the treatment of multiple myeloma," he added.

DURABLE RESULTS

Study results, which were presented at the 2021 American Society of Hematology (ASH) annual meeting, demonstrated an objective response rate (the rate of measurable response to treatment) of 97.9%. Additionally, 82.5% of patients achieved stringent complete response and 94.9% achieved a very good partial response (a decrease in tumor size or the amount of cancer in the body as a response to treatment) or better.

"This study shows the highest response rate in these patients that's ever been achieved," Martin said.

He explained that only two patients did not qualify as having a response, and one of them was deemed as having unmeasurable disease in the beginning. However, that patient still remains in remission. "Honestly, there's only one patient who perhaps did not have a response to this therapy. (This is) amazing in this really heavily pretreated population," he said.

The median time to first response was one month, 2.6 months to best response and 2.9 months to complete response or better. The median duration of response was not estimable. And of 61% of patients who were evaluable for minimal residual disease (MRD; the small number of cancer cells in the body after treatment), 91.8% were negative.

The 18-month progression-free survival (or time during and after treatment when the patient lives without disease progression) was 66%, and for those who sustained MRD for at least six months and at least 12 months, it was 96.3% and 100%, respectively. The overall survival rate (patients with cancer who are still alive after treatment) was 80.9%.

Results demonstrated that 60.5% of patients remained in remission at a 24-month follow-up. Martin said the average remission duration is going to be more than 24 months and may approach 30 months or beyond.

"What we showed at the ASH meeting was that responses were again durable, essentially lasting longer than any other therapy tested in this relapsed/refractory population. … This is really dramatic and the best responses and the best »

results … we've ever seen in this population," he explained.

SIDE EFFECTS

The most common severe side effects occurred in at least 25% of patients and included low white blood cell counts such as neutropenia (94.8%), leukopenia (60.8%), thrombocytopenia (8%), lymphopenia (49.5%) and anemia (68%).

Martin said that patients are often apprehensive because the side effects can be significant. However, when he asks patients which had worse side effects, the CAR-T cell therapy or autologous stem cell transplant, they uniformly say the transplant.

Mild or moderate cytokine release syndrome (when a particular protein overstimulates the immune system so that it attacks healthy organs) occurred in 94.8% of patients but was resolved within two to seven days with medicines, Martin said, compared with side effects from a transplant, which can last one to three months.

"I don't worry so much about the side effects. We have great treatments, and we generally have ways to mitigate all the side effects of CAR-T cell therapy," he added.

Martin explained that prior to CAR-T cell therapy, patients receive chemotherapy that suppresses the immune system to create room for the incoming T cells, also contributing to the ongoing immunosuppression. But it is necessary for T-cell expansion and allows the T cells to better kill the myeloma.

"I tell people that the initial chemotherapy acts to rid the 'immune bunkers' that are sitting all over your body and in lymph nodes, bone marrow, etc., to make space for those CAR-T cells, which grow and amplify in those bunkers and then kill the myeloma cells," Martin said. "We have to do this chemotherapy, but it also makes people's immune system quite low."

When CAR-T cells are given, they are strictly focused on targeting myeloma, not other infections such as the flu or COVID-19. Additionally, the CAR Ts can knock off normal plasma cells, and these cells make antibodies to protect one's body against viruses. Many of these patients require supplemental intravenous gamma globulin infusions (IVIG) in the first six months of CAR-T cell therapy and will also utilize antibiotics to help prevent a shingles reactivation or pneumonia.

"The first three to six months after a CAR-T (therapy), people are at risk for infection and we want them to just be careful. … Patients feel well and feel like doing a lot of stuff, but in today's world, they have to focus on being safe and staying local. … Patients can certainly go outside, can still exercise and spend time with family but need to discuss additional freedoms with their CAR-T cell providers," he said.

LIMITATIONS AND OPTIMISM FOR THE FUTURE

One downside to CAR-T cell therapy is that it is recommended that patients visit a cancer center with experience in administering these treatments. There are only 70 to 100 of those in the United States, so not everyone has access to it, Martin said. It's also not an "off-the-shelf" therapy; thus, it takes time to prepare and manufacture the CAR-T cells. In fact, it could take up to four to six weeks, and some patients cannot wait that long for this therapy.

However, Martin said, this is not the only therapy that is performing well in this patient population, and there is much to look forward to.

"What's exciting is that now we (have) many other immune therapeutics that are being developed in this patient population. Many are being tested in phase 1 trials, but several have progressed to phase 2. Most exciting are the T-cell-engaging antibodies, where one arm of the antibody targets and anchors the antibody to a protein on the myeloma cell surface like BCMA, and the other arm binds to and activates T cells in the local environment. The activated T cells kill the myeloma cells. These agents are showing remarkable responses and thus optimism for their use" he said.

He said these other therapies can take the place of CAR-T cell therapy, especially for those who don't have access or may not be fit enough for CAR-T cell therapy. Early results suggest that patients can still achieve a deep remission with these T-cell-engaging or bispecific antibodies.

Martin remains very optimistic about the future of multiple myeloma treatment because of these early positive results. All the currently approved drugs for multiple myeloma have previously shown single-agent responses rates between 20% and 30%; that was the previous bar for drug development, Martin said. So, to have this CAR-T cell therapy show responses rates greater than 90% as a single agent is a big advance for myeloma. Other studies testing different CAR-T's have also demonstrated good results with response rates between 80% and 90%. He also highlighted bispecific T-cell-engaging antibodies, which are demonstrating single-agent response rates between 55% and 85%.

"This is a whole new level of activity with all of these new drugs and therapies," he added.

Martin explained that when they test these drugs in patients with refractory disease and it works so well, they want to bring it to earlier lines of therapy. So, these drugs are now being used in patients who previously received one to three lines of therapy, and soon they will be tested in newly diagnosed multiple myeloma, he said. Martin noted the future is quite bright for these therapeutics throughout the myeloma treatment continuum.

"I don't think there's ever been a time in myeloma therapy where we have such optimism for our next generation of drugs," he concluded.

PSYCHOLOGICAL

Anxiety and Depression May Deter Patients From Joining Clinical Trials

Psychological side effects may skew patients' perceptions of trials.

By COLLEEN MORETTI

PATIENTS WITH MULTIPLE MYELOMA often do not participate in clinical trials and may have a skewed perception of them because of anxiety and depression, according to results of a recent study.

Neha G. Goyal, a staff psychologist at UCSF Helen Diller Family Comprehensive Cancer Center in San Francisco, told *CURE*® that patients with multiple myeloma often experience anxiety and depression because of their disease. Multiple myeloma can be a treatable cancer, but it is considered incurable, which can bring up many different emotions because of the uncertainty, she explained.

"Even in those periods where people are not in treatments, there is this ongoing uncertainty or fear of … relapse that can make one feel anxious. So even when (patients) are on treatment (or) off treatment, there are these fears or thoughts that are coming up that can really contribute to anxiety," Goyal said. "We see this in other cancers, but I think there's a unique aspect of multiple myeloma that make one more prone to feeling some of these emotions of anxiety and sadness."

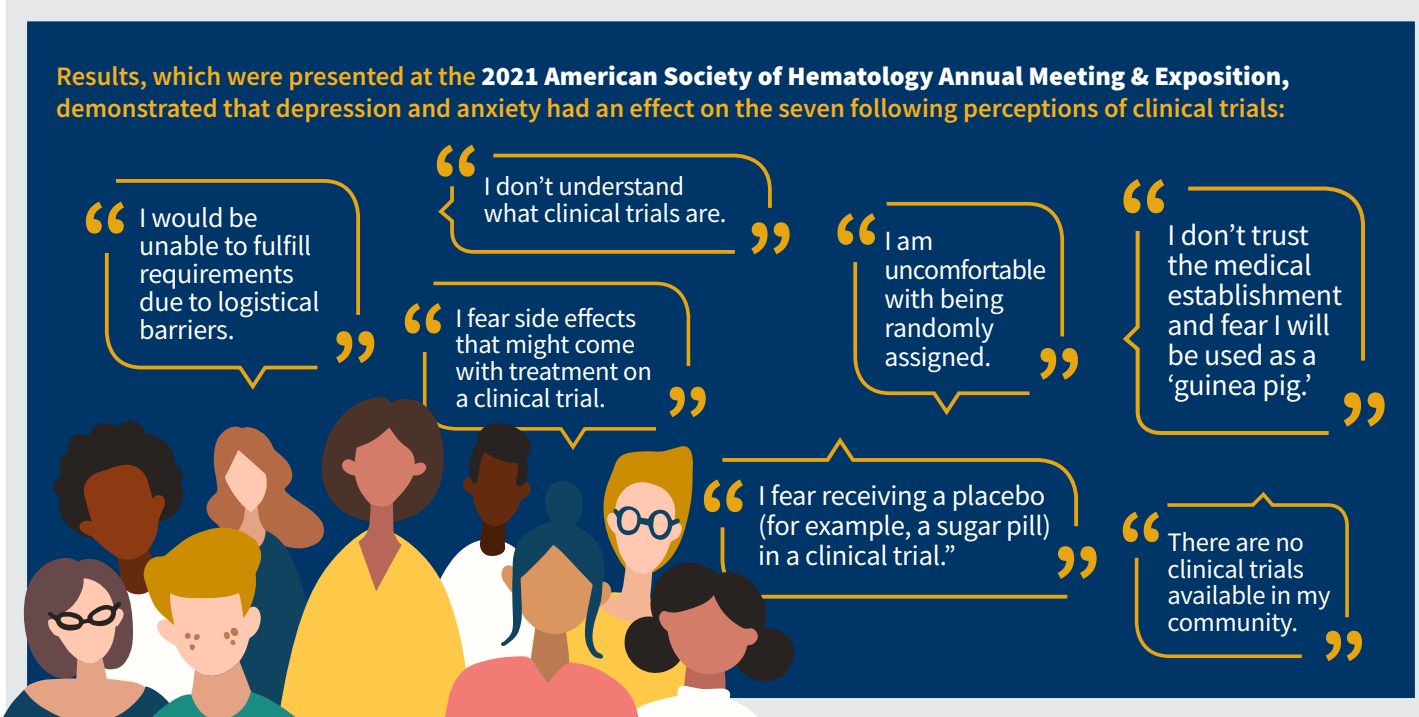
PERCEPTION OF CLINICAL TRIALS

Psychological side effects such as depression and anxiety can influence a patient's everyday life, Goyal explained, so could it also affect their ability or desire to participate in a clinical trial?

Kimberly Papay Rogers, director of research at Cancer Support Community and lead author of the study, explained in an interview with *CURE*® that there are thousands of clinical trials, with a main goal to improve patient outcomes and increase quality of life. However, participation remains low, so it is important to understand the barriers patients might face regarding perception and participation.

"A lack of participation in clinical trials can really prevent progress in these areas. And obviously better outcomes are of the utmost importance to patients and their families and health care providers. Engagement in clinical trials is really crucial to keep progress moving forward," she said.

The study included 625 patients with hematologic cancer, mostly multiple myeloma (46.4%), who completed an online survey to assess their perception of clinical trials and measure anxiety and depression. Patients (median age, 60.1 years) were mostly female (54.9%) and non-Hispanic White (86.7%). »



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These findings shed light on fears and perceptions that patients are feeling, Rogers said. For example, many patients are worried about receiving a placebo. However, most trials are not placebo controlled. Instead, new treatments are compared with the standard of care, she said.

Interestingly, the study also demonstrated that these perceptions were higher among those who had higher levels of anxiety and depression, but more research is needed to fully understand why these relationships are observed and what they mean. Rogers did point out that "in this survey sample, 21% of patients had elevated levels of anxiety and 27% of patients had elevated levels of depression, which is higher than what we see among adults in general in the United States."

Goyal explained that feelings of anxiety can make a person worry about the "what ifs" — for example, "What if the trial doesn't work?" "What if I have unexpected side effects?" These uncertainties are "a breeding ground for anxiety," she said, and patients might rather go down a path, or treatment, that is more well known.

"As this study so nicely pointed out, when we are feeling depressed or when we are feeling anxious, we have certain perceptions, (and) we view the world in a certain way when we're feeling more anxious and depressed. And so those negative perceptions can also impact one's willingness to join a trial," Goyal said.

THE IMPORTANCE OF UNDERSTANDING

Both Goyal and Rogers agree it is important to understand the factors and barriers to participating in a clinical trial. These trials allow for advancements and new treatments in myeloma and other cancers.

"It's important to understand what the reasons or barriers are to patients participating in clinical trials … to be able to directly address those barriers so that we can get more patients into these clinical trials and it can sort of … speed up the process in the development of these treatments and (then) those treatments coming out on the market for other patients," Goyal said.

Rogers says that is what the study allowed them to do.

"I think it's important to recognize the end goal is always to minimize barriers that may stand in the way of people accessing clinical trials. But we can't really work to minimize those barriers until we understand them better. That's what this study was about and why we feel it's so important," Rogers concluded.

COMMUNICATION

Triple-Class Refractory Myeloma Requires 'Greater Attention to Symptoms'

To address symptoms from myeloma that is resistant to treatment, education and communication with care teams are key.

By COLLEEN MORETTI

PATIENTS WITH TRIPLE-CLASS refractory multiple myeloma (when the disease does not respond to immunomodulatory drugs, proteasome inhibitors and anti-CD38 antibodies) are likely to have significant hospitalizations and a clinically meaningful decline in health-related quality of life; according to a recent study.

Lynne I. Wagner, one of the study's authors and a professor in the Department of Social Sciences and Healthy Policy at the Wake Forest School of Medicine in Winston-Salem, North Carolina, said this study is important for patients because the results highlight the need for paying greater attention to symptoms.

"(These results) indicate that these patients, when they transition to a triple-class resistant disease, may benefit from greater clinical attention to offer symptom palliation (and) greater clinical attention to address some possibly modifiable factors to maximize their quality of life," she said in an interview with *CURE*®.

The study, results of which were presented at the 2021 American Society of Hematology Annual Meeting & Exposition, included 240 patients with multiple myeloma who had become triple-class refractory.

During the follow-up period, hospitalization for any reason and multiple myeloma-related hospitalizations occurred in 49.6% and 23.8% of patients, respectively.

There was also a significant decline in health-related quality of life from the beginning of the study to the follow-up period, as indicated by clinically meaningful deterioration in patients' physical and functional well-being and myeloma-related concerns, Wagner said. This means these patients had worsening pain and a decreased overall health rating of themselves.

In addition, patients whose multiple myeloma is less controlled and who have more health-related issues have not only their physical and functional well-being affected but also their emotional and social well-being, she said.

Wagner added that when a patient's disease is resistant to treatment or their multiple myeloma is triple-class refractory, it is important to remain educated about other treatment options.

"Confidence in one's ability to manage one's health and to manage one's myeloma will be really important for patients who find themselves in this scenario, so they gain a greater sense of control by learning more about treatment options and engage in that important dialogue with (their) provider and their health care team with regard to treatment decision-making," she said.

Results from the study demonstrated that patients who received subsequent lines of therapy (64%) had a median overall survival (time from diagnosis or treatment start when patients are alive) of 10.8 months, whereas those who did not receive additional therapy (35%) had a median overall survival of one month. However, Wagner noted that this was not a randomized trial, so those participants (35%) may have had

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a poorer health status or were too frail to receive additional lines of therapy.

"This does suggest that patients should engage in a very important conversation with their oncology team about … the toxicities that will be introduced by any additional lines of therapy, with improved survival (as the) trade-off," she said.

She noted that if a patient tells their health care team about their pain, the team can implement effective interventions to relieve it. Additionally, learning coping strategies to handle uncertainty is important, she said, because having treatment-resistant disease can cause psychological distress, affecting one's quality of life. There are coping strategies patients can learn to manage uncertainty and reduce distress, so they can maximize their quality of life in the face of a challenging disease.

"I think for the patients (whose disease is refractory to) treatment … communicating with (their) health care team about deteriorations and (their) health-related quality of life is critically important," she concluded.

ANOTHER 'TOOL IN THE TOOLBOX'

Patients with relapsed/refractory disease may be able to switch to Darzalex Faspro after their first relapse or if other treatments are not working.

By BRIELLE BENYON

ALTHOUGH DARZALEX (daratumumab) plus Kyprolis (carfilzomib) and dexamethasone is a commonly used myeloma regimen that was approved in August 2020, the Food and Drug Administration (FDA) more recently approved Darzalex Faspro (daratumumab plus hyaluronidase-fihj) in combination with Kyprolis and dexamethasone for the treatment of adults with relapsed/refractory multiple myeloma who previously underwent one to three lines of treatment.

The recent approval is a "technicality," said Donna Catamero, associate director of myeloma translational research at Icahn School of Medicine at Mount Sinai in New York City, in an interview with *CURE*®, explaining that Darzalex Faspro is the subcutaneous formulation of the drug. It is given via injection rather than intravenous infusion, as traditional Darzalex is administered. Many institutions were already using this method for their patients, Catamero believes.

"This combination is exciting as it can be used with a patient's first relapse," Catamero said. "Updated data were presented at the (American Society of Hematology) 2021 Annual Meeting and Exposition … which showed with longer follow-up, patients had improved progression-free survival."

Findings from the PLEIADES clinical trial led to the approval of the Darzalex Faspro regimen. In patients with pretreated relapsed/refractory myeloma, 84.8% responded to treatment, with the majority of patients — 85.2% and 82.5% — still responding at the six- and nine-month marks, respectively, the trial results showed.

Catamero, who is a board-certified adult nurse practitioner and certified oncology nurse, explained that this could be a good option for patients to switch to a different type of therapy after discovering one type of treatment is not working.

"Patients can discuss this option with their physicians, as this combination offers a class switch if (a patient's disease is) progressing on Revlimid (lenalidomide) maintenance," she said.

However, as with all cancer treatments, there are side effects to be aware of, including severe or fatal heart complications such as heart failure or hypertension that have previously been linked to Kyprolis.

"The side effect is rare; however, patients with preexisting conditions may be at higher risk," Catamero added. "Patients who do receive this combination should discuss how their cardiac function will be monitored during treatment."

Other common side effects observed in the PLEIADES trial were upper respiratory tract infection, fatigue, insomnia, high blood pressure, diarrhea, cough, difficulty breathing, headache, fever, nausea and peripheral edema (swelling of the lower legs and hands).

"Overall, this is an exciting new option," Catamero concluded. "This gives us more tools in our toolbox."

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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 Mount 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 $3.5 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.

After pausing for the global pandemic, we are back with a new schedule of exciting climbs. Patients, caregivers, loved ones with myeloma, and others impacted directly by multiple myeloma will trek through the wilderness of Alaska's Kenai Peninsula, summit Mount Washington and discover the dynamic terrain of Colorado's Backcountry Continental Divide. 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:
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patient
spotlight

‘Fighting Cancer *One Outfit* at a Time’

Donna McNutt uses her love of fashion to find confidence and motivation — and shares it with others. *By* COLLEEN MORETTI

DONNA MCNUTT KNEW SOMETHING was wrong when she woke up Easter morning 2015 and couldn’t do the one thing she always does, no matter what: get dressed.

This was extremely unlike the woman known by friends, family and now more than 5,000 Instagram followers as “the cancer fashionista.” In an interview with *CURE*®, McNutt shared how she uses her Instagram account as a way to find confidence and motivation, and connect with other people going through similar cancer journeys.

RECEIVING HER DIAGNOSIS

In 2015, McNutt was living in a small cottage in Laguna Beach, California, with her husband, Jack. Her three children were grown, leaving her and her husband in an empty nest — something they were excited about.

“My life was really full, going into those really fun years of when your responsibility for your family is slowed down. And then, cancer,” she said.

For three months she had not been feeling great. She had been experiencing bad rib pain, which she thought was from dancing on Friday nights at a local bar with her husband. But that Easter morning she told him to rush her to the emergency room. She would be there for two weeks and later received a diagnosis of multiple myeloma.

Hearing those words was easier to absorb in that moment than it would have been sitting in an office, she said. She felt she had just finally let go of everything she had been holding in for the past three months.

“For me, I didn’t even care (whether) they told me I had an alien living inside me. It was just like, ‘Oh my gosh, please take care of me,’” she said.

After leaving the hospital, she felt like a mere shell of her previous self. Her kidneys were failing, and she couldn’t even fit into her underwear anymore.

PASSION FOR FASHION

When she returned home and started going to treatment appointments, she felt unattractive and wondered what she could do to make herself feel better. She was always worried that her cancer would strip away what she loved most: fashion. So she started putting in the effort and getting dressed up for chemotherapy and doctors’ appointments.

“It wasn’t really a conscious decision of, ‘Oh I’m going to look like this in chemo or going to the doctor’s office,’” she explained. “That’s who I am. And I’m not going to let cancer take that from me.”

However, it was a slow process. Many of her clothes didn’t fit right, so she got rid of all the clothes that fit her old life but not her new one.

So, it started with a pretty pashmina scarf she would wear during her six months of chemotherapy while preparing for a stem cell transplant.

And then every day she felt good, she would take a photo of herself leaving the doctor’s office or going to chemotherapy and send them to her family to keep them updated.

“Not only am I someone’s wife, someone’s mom, I’m someone’s daughter, I’m someone’s sister going through cancer,” she said. “I started snapping pictures and sending them to my family. ‘Look at me today. Look at me.’ That was my message to them. What better way for them to believe that I was fighting and I was getting better than getting dressed. And it just started from there.”

And so, McNutt became the cancer fashionista.

THE CANCER FASHIONISTA

When she entered into City of Hope in Duarte, California, for her treatments, scans and appoint-

Getting dressed every morning for appointments and everyday life keeps **DONNA MCNUTT** motivated through her journey with multiple myeloma.

PHOTOS PROVIDED BY DONNA MCNUTT

ments, she felt she was taking cancer on as she walked down the hallway.

Soon, McNutt said, she became known as the woman about whom everyone asked, "Oooo, what does she have on today?"

And she transferred that energy to Instagram with her profile bio, "Fighting Cancer One Outfit at a Time!" Here she shares her outfits of the day and what she's up to — whether it's getting a bone marrow biopsy or just enjoying the California weather. It's all done with the help of her husband, who takes the photos.

"I didn't really know much about Instagram, but I just knew I have to share (and) that you have to keep your 'thing.' I *kept* my thing," she explained.

Patients with cancer already have a lot of pressure on them and McNutt wanted to be sure that her Instagram didn't add any more pressure on anyone to feel they have to look put together and have the best outfit for treatments. She just wants them to know that they should continue doing what they love, just as she is.

"You're so into blaming yourself that I wouldn't want the pressure to be, 'Look at that woman, I'm never going to be her.' I want them to really, truly, authentically understand that," she said. "I love this and this is me fighting cancer one outfit at a time — find what *you* want to fight cancer with one something at a time."

McNutt added that she is not an influencer. Although she has had opportunities, she does not have sponsored posts. It doesn't matter to her how many followers she has. She wants them to follow her to see something different and authentic.

"I feel so blessed because my followers have helped me, too. Because there are plenty of days I really don't want to get dressed. I want to give up. Now I have kind of a responsibility," she said.

FINDING CONFIDENCE WITH CANCER

Many patients can lose their confidence after having cancer or as they are going through treatment. McNutt said patients with cancer should find what made them feel confident before receiving a cancer diagnosis and tap into that.

"You are the person you were the day before cancer," she tells other patients.

She recalled how she experienced body image issues.

"I think that has to come with an acceptance of everything (in) your scenario. I am much better at that today than I was six years ago," she said.

McNutt has found her motivation and energy every day through getting dressed and making sure she has something to do. McNutt found she had a lot of time at home, especially after her stem cell treatment and chimen antigen receptor (CAR) T-cell therapy. She is currently letting her new CAR-T cells do their job and is praying for a long remission while she looks for things to do around the house that keep her going — whether it's writing to a pen pal or cleaning out her closet or crafting.

She tells others that whatever they are doing that day to put all their heart into it.

"I just don't want to languish here in a pair of sweatpants," she said.

To hear **MCNUTT** speak more about how she found confidence in fashion, **SCAN THE QR CODE AND LISTEN IN!**

heal
at home

How a Nutritious Diet May Help During Treatment

Maintaining a healthy diet during treatment may help combat side effects.

By RAYNA MCCANN, M.S., RDN, CSO, CDN

ALTHOUGH IT IS SOMETIMES overlooked, nutrition is a pivotal factor in a patient's medical plan.

Receiving adequate nutrition before, during and after treatment can help with side effects, quality of life, strength, fatigue, healing, treatment toxicities and so much more.

Depending on the cancer diagnosis and treatment plan, nutrition recommendations may change. Common symptoms of multiple myeloma may directly affect nutrition, both before diagnosis and after.

ELEVATED CALCIUM LEVELS

Approximately one in three people with cancer has high calcium levels, known as hypercalcemia. High calcium levels are common in patients with multiple myeloma. The high levels usually are not due to consuming large amounts of milk or calcium-rich foods but instead are the effect of the cancer on the bone. If the calcium level is high, a patient may be told to not consume a lot of dairy products. At the same time, it's important to take in enough fluids to help the kidneys remove excess calcium from your body.

RENAL OR KIDNEY FUNCTION

Multiple myeloma also may affect renal or kidney function. Kidney damage is common in patients with multiple myeloma, and it can lead to elevated potassium and/or phosphorus levels. Patients should communicate with their medical team to stay aware of potassium and phosphorus levels when their blood work is taken.

If laboratory results show elevated levels, a patient may need to cut back on foods that are high in potassium and/or phosphorus. In the ingredients list, look for words such as "dicalcium phosphate," "disodium phosphate" and others to identify additives.

Foods that are high in potassium include bananas, oranges, cantaloupe, apricots, prunes, raisins, dates, potatoes and avocados. Foods that are high in phosphorus include dark colas and dairy products such as milk, ice cream and pudding.

SIDE EFFECTS

During treatments, a patient may experience a wide range of side effects that affect nutrition, such as nausea, constipation, loss of appetite, fatigue, weight loss and excessive thirst. These may affect daily life, but there are some ways to combat these.

NAUSEA

Having nausea can greatly affect nutrition status. Identifying patterns may help to guide treatment, so patients should keep their medical team informed. For example, if a patient experiences nausea every night before treatment, it may be caused by anxiety, as opposed to nausea following treatment, which may be caused by the medication.

TIPS TO CONTROL NAUSEA

1. Consume foods at room temperature. Hot foods can increase taste and aromas, which may worsen nausea.
2. Avoid the kitchen when food is being cooked if smells bother you. Open windows to help with ventilation. Drink liquids through a cup with a lid and straw to lessen potent smells as you drink.
3. Try travel acupressure wristbands, such as Sea-Bands.
4. Use guided imagery or meditation to reduce anxious thoughts, which may cause nausea.

CONSTIPATION

Constipation can also be a sign of high calcium level, along with dehydration, thirst, confusion and worsening of underlying bone pain — so this should be pointed out. Fiber, or roughage, can help prevent constipation, but that's only part of the story. Eating high-fiber foods such as spinach, whole grains and beans can help with bulk, but adequate hydration is also vital. Consuming enough fluids helps move bulk throughout the body and rid the body of waste. Drinking warm fluids in the morning may help ease constipation. A patient should tell their medical team how often they have bowel movements, in case a bowel regimen is needed.

UNINTENTIONAL WEIGHT LOSS

More often than not, the number on the scale does not tell the full story. If a patient gets fatigued during daily activities, such as opening a jar or walking to the mailbox, they may be showing signs of muscle wasting. Patients should tell their medical team if they feel they have lost muscle mass and/or have lost weight without trying. A registered dietitian can show how to add nutrient-dense foods to the diet and explain ways to rebuild or preserve muscle mass, such as strength training and adequate protein intake.

NEUTROPENIA

Neutropenia is a term used to describe low neutrophils, a type of white blood cell. Having neutropenia may increase the risk for infection. Because of this risk, a medical team may discuss specific diet guidelines to avoid harmful organisms from foods and beverages. Safe food handling is especially important if a patient is receiving chemotherapy or radiation, or has had a stem cell transplant.

BASIC DIET RECOMMENDATIONS

1. Avoid rare/undercooked meat, fish or eggs. Cook all until well done.
2. Avoid unpasteurized beverages such as raw milk or fruit juice.
3. Avoid buffets or open container grab-and-go stations.
4. Avoid soft mold-ripened or blue-veined cheeses such as brie, Gorgonzola or blue. Avoid all unpasteurized cheese/dairy products.
5. Wash and cut all fruits and vegetables yourself, and wash them before peeling to avoid contamination from bacteria.

KEEPING TRACK

Patients should bring a notebook to appointments. Their medical team may mention certain foods or beverages that need to be avoided with medication, such as grapefruit or green tea. They also may give instructions about taking medication on an empty stomach or with food. All of this information may feel overwhelming. It can help to bring a support partner for a second set of ears or to take notes.

Nutrition should be part of a patient's treatment plan, and it should be tailored to their specific laboratory results, medications and condition. Ask to speak with a registered dietitian for guidance on how to best fuel the body.

20 YEARS *of* Treatment, Quality-of-Life Advances

In honor of *CURE*®'s 20th anniversary, we spoke with experts on how the past 20 years have revolutionized multiple myeloma treatment.

By COLLEEN MORETTI

ADVANCEMENTS IN THE treatment of multiple myeloma over the past 20 years have significantly affected the lives of thousands upon thousand of patients.

"The survival of (patients with myeloma) has more than quadrupled over the past 20 years, and we've come from conventional chemotherapies to targeted novel therapies," said Dr. Saad Z. Usmani, hematologic oncologist and chief of myeloma service at Memorial Sloan Kettering Cancer Center in New York City, in an interview with *CURE*®.

TREATMENT ADVANCEMENTS

When Usmani was a trainee, there were only two classes of drugs for patients with multiple myeloma in their first line of treatment: immunomodulatory drugs (IMIDs) such as Thalomid (thalidomide) and Revlimid (lenalidomide) and the proteasome inhibitor (PI) Velcade (bortezomib). Then came the next-generation immunomodulatory drug Pomalyst (pomalidomide) and second-generation proteasome inhibitors Kyprolis (carfilzomib) and Ninlaro (ixazomib).

The real revolution started in 2010, when there was a bigger focus on immune-based treatment approaches such as targeting specific surface antigens, chimeric antigen receptor (CAR) T-cell therapy and bispecific antibodies.

DR. SAAD Z. USMANI

"All of those therapies just really propelled and started to change the landscape of myeloma treatment," he said.

Usmani added that conversations among doctors also started changing over the years, and they realized that combining drugs could lead to better survival outcomes. As a result, combination therapies began penetrating the space around 2015 and 2016, he noted. And now the standard of care in the second-line treatment of patients with relapsed multiple myeloma is three-drug combinations known as triplets.

"I think we have better tolerability for these therapies in myeloma compared to the conventional chemotherapies. We have better responses (and) better survival outcomes," he explained. "We have learned to (treat) patients more effectively over time, manage side effects better with dose adjustments and alternate schedules, and because of these advances we also have a lot of … younger hematologist oncologist trainees who have shown interest in doing quality research in this disease. (There) has been an influx of good, fresh ideas, as well, over time."

Dr. Gurbakhash Kaur, an assistant professor of internal medicine at UT Southwestern Medical Center in Dallas, has been specializing in multiple myeloma for three years. Although she was not "in the trenches treating

MARINA ZLOCHIN / STOCK.ADOBE.COM

patients" at that time Usmani was, she agrees that the advancements for treating multiple myeloma have been significant over the years.

She also noted that 20 years ago, IMID- and PI-based therapies were not even approved for multiple myeloma. Since then there have been over 16 drug approvals for multiple myeloma. which researchers reported at the 2021 American Society of Hematology Annual Meeting and Exposition.

"The type of therapy you choose for second line takes into account patients' comorbidities, preferences and quality of life. Treatment at any stage of relapse of myeloma is important, and you have to make the most informed decision and the right decision for the patient," she explained.

Kaur mentioned the increased use of the combination of CD38 antibodies like Darzalex (daratumumab) and Sarclisa (isatuximab), CD38 antibodies and second-generation PIs such as Kyprolis and Ninlaro with newer immunomodulatory agents like Pomalyst are used mostly in the second line.

QUALITY-OF-LIFE ADVANCEMENTS

Usmani and Kaur have seen significant improvements in quality of life, something they both said is important for their patients.

"The patients are at the center of (it) … they are the central keys to everything that we do," Usmani said. "When I meet with patients, I tell them … the patient is the most important person in the room. These advancements and all these new data are helping us manage our patients better, take care of them better, give them the opportunity to have a better quality of life, to do things that really matter (and) to spend time with their loved ones."

He added that over the years, doctors have come to understand that myeloma is typically a disease of older age. Treatments today are better tolerated for older patients than past conventional chemotherapies. The safety and side effect profiles are also better, which translates to a better quality of life.

> To me, that's the most amazing thing about the advancements we've made, that we as myeloma physicians … are starting to address the quality of life questions a lot more than before. — DR. GURBAKHASH KAUR

For example, infusing Darzalex used to take eight hours, and Kaur would dread having to tell a patient they would have to go through that. Over the years the process has been dramatically shortened, and now administration is a shot under the skin and takes only five minutes.

"That itself has changed patient's experience and quality of life, and I don't even blink when I have to introduce (Darzalex) to a patient anymore," Kaur noted.

She said that physicians now have a "luxury" of options that were not available before, meaning that if a patient does not want to receive an intravenous infusion, there may be an oral option instead. For patients in treatment, a main focus is on toxicities and quality of life, which explains how far management of the disease has come in 20 years.

"To me, that's the most amazing thing about the advancements we've made, that we as myeloma physicians … are starting to address the quality-of-life questions a lot more than before," Kaur said.

THE NEXT 20 YEARS

Usmani and Kaur agree that immunotherapies, such as bispecific antibodies, and CAR-T cell therapies are the future for managing multiple myeloma. Currently, these therapies target a surface marker on myeloma cells called B-cell maturation antigen, or BCMA, but other surface targets are on the horizon.

Usmani added that new cell modifications and biomarker-driven treatments, such as Venclexta (venetoclax), will become important players in the second-line treatment of relapsed disease. He said important metrics in these new treatments include whether they are safe for the patients, are effective in a deeper response or lead to better progression-free survival (or the time during and after treatment when the patient lives without disease progression).

Kaur added that the ultimate goal is to have a treatment that is curative, and with these new immunotherapies doctors might be able to get there. She is hopeful for the future of patients with multiple myeloma, but she said there is more work to do in understanding how to sequence new treatments.

"I do have quite a bit of hope of these newer agents moving further up front. … Myeloma, there is a science to it, an art to it, which is the personalized aspect of it. … What we need to figure out (is) how to sequence these medications and have a more scientific approach. … What are the right combinations? We're still figuring out those (answers), but that's my hope for the future," Kaur concluded.

TREATING BONE PAIN IN MULTIPLE MYELOMA

Bone pain is a common symptom that patients with multiple myeloma face, but some may find relief with treatments and exercise.

By ARLENE WEINTRAUB

In 2017, Michael Padjen was on the job at his exterior cleaning company in Greensboro, South Carolina, when he jumped off the bed of his truck and felt pain in his back. A course of steroids didn't help, so he went for an MRI, which showed not only a severe compression fracture in one of his vertebrae but also abnormalities in his bone density.

A blood test then uncovered the reason behind Padjen's back pain: multiple myeloma. "Within the next seven weeks, I (developed) seven severe compression fractures, all in my back," Padjen says.

However, Padjen's story is not uncommon.

For Kenny Capps, a lifelong runner and all-around endurance athlete who lives in Black Mountain, North Carolina, the first sign that something was off came in 2014. "I started having issues with fatigue after long events. I thought I was getting the flu," Capps says. "I had serious back pain, but I assumed I had just pulled something." After Capps received a diagnosis of multiple myeloma, positron emission tomography (PET) scans revealed two compression fractures in his spine, a lesion in his hip bone, and bone loss in his collarbone, sternum and skull. »

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Bone pain is a main symptom of multiple myeloma because the cancerous plasma cells that cause the disease can also weaken bones. The result is not only pain but also an increased risk of weakness and bone fractures. A 2020 study of more than 800 patients with multiple myeloma found that bone pain led to the diagnosis in 63% of patients, and that 74% of patients had two or more bone lesions by the time they started their multiple myeloma treatments.

The good news is that the entry of new multiple myeloma drugs to the market — 12 in the past 15 years, according to the Multiple Myeloma Research Foundation — has raised the probability that patients with new diagnoses will achieve remission and, by extension, relief from their bone pain.

"Most people who present with multiple myeloma have bone pain. It's the most common symptom," says Dr. Shagun Arora, a hematologist-oncologist at the University of California, San Francisco. "Our first goal is to control the cancer as fast as possible. Typically, if the myeloma is responding well, pain starts improving and we know the bone disease is getting better."

SALLY GUPTON

UNDERSTANDING THE PAIN

Multiple myeloma weakens bones by disrupting the normal balance between osteoblasts, which are bone-making cells, and osteoclasts, which break down bone. "The myeloma cells release signals that affect the bone marrow microenvironment in a way that increases the breakdown of bone," says Dr. Carlyn Tan, a hematologist-oncologist at Memorial Sloan Kettering Cancer Center in New York City.

The result can be pain that spans a wide spectrum, from a dull ache that's set off by certain movements to severe pain caused by a fracture. Sometimes multiple myeloma forms tumors called plasmacytomas, which can appear in bone or surrounding soft tissues, causing pain. Some patients develop pinched nerves or spinal cord compression due to involvement of the vertebral bodies, which are the bones that support the body and protect the spinal cord. That can cause shooting pain down the legs, paralysis, incontinence and other problems.

Finding the source of bone pain is an important step in diagnosing multiple myeloma, Arora says. That's because some bone issues need to be treated immediately to reduce the risk of breakages or compression fractures. For example, weakened bone segments, referred to as osteolytic lesions, are common in multiple myeloma, but when they occur at locations such as the top of the femur, they can be dangerous. "Myeloma involvement can lead to fragile bones, and simple movements like walking can lead to painful fractures," she explains.

Oncologists typically start with "head to toe" imaging, Arora says, which can include low-dose CT scans, PET/CT scans or MRIs. Surgery and radiation can alleviate osteolytic lesions as well as plasmacytomas that could otherwise endanger the spinal cord, Arora adds.

Once patients start their drug treatments for multiple myeloma, they're typically prescribed bone-strengthening treatments simultaneously. One option is Zometa (zoledronic acid), which is in a class of medicines known as bisphosphonates, also used for osteoporosis (thinning of the bones). They work by inhibiting bone resorption, or breakdown. Zometa is given by infusion once every one to three months. Bisphosphonates sometimes cause mild side effects such as flu-like symptoms, flare in bone pain, itching and numbness, but the advantages often outweigh the risks, Tan says.

"Using (Zometa) prevents future fractures and has been shown to help with bone pain also," Tan notes. A 2017 analysis of four studies involving 601 patients with multiple myeloma concluded that patients who took bisphosphonates faced a lower risk of nonvertebral fractures than did those who were not prescribed bone-directed drugs.

Padjen, now 64, was treated with the standard multiple myeloma triple-drug regimen of Velcade (bortezomib), Revlimid (lenalidomide) and dexamethasone. He also was treated with Zometa. Then he received a stem cell transplant. But his back was in such bad shape he had to undergo three »

KENNY CAPPS was struggling with bone pain because of multiple myeloma but found some relief in treatments and exercise.

operations prior to the transplant and one after, including kyphoplasty.

For patients such as Padjen who have significant back pain and fractured vertebrae, kyphoplasty can stabilize the backbone and offer significant relief. During this procedure, a balloon is inserted into the collapsed vertebra and inflated, creating a space. Then bone cement is injected into the space.

Capps, now 50, also received the same regimen of Velcade, Revlimid and dexamethasone, followed by a bone marrow transplant. This put him into partial remission, and he remains on a maintenance therapy. He also was prescribed Zometa for his bones, and he undergoes PET scans to monitor his bone health twice a year.

Another option for preventing bone issues in multiple myeloma is Xgeva (denosumab), an antibody drug that decreases bone resorption by inhibiting a protein that controls the survival and functioning of bone-destroying osteoclasts. Results of a 2018 study, published in *The Lancet,* comparing Zometa with Xgeva in patients with newly diagnosed multiple myeloma with at least one lytic lesion found that Xgeva matched Zometa's effectiveness in preventing skeletal-related events.

Zometa, however, can exacerbate kidney issues, with some patients experiencing

CARRIE TURNER

renal injuries or failure while on the drug, so Xgeva may be a better choice for patients with chronic kidney disease. Xgeva is also more convenient, in that it can be given as a subcutaneous injection every four weeks, Tan says. Both Zometa and Xgeva can cause a degeneration of the jaw known as osteonecrosis. So patients are advised to visit a dentist to check the health of their jaw bones prior to starting the medication, she adds.

RELIEVING THE PAIN

Oncologists who treat patients with multiple myeloma often prescribe bone-strengthening supplements to their patients, including vitamin D and calcium. But because the breakdown of bone can cause calcium to be released into the bloodstream, physicians typically run blood tests to measure patients' calcium levels before recommending a supplement regimen, Arora says.

"If calcium levels are high, we need to treat the cancer first and get that under control so calcium levels will start normalizing," Arora says. "Then our next step is to help the bones restructure themselves. Then we add in the calcium and vitamin D."

Exercise is also an important component of multiple myeloma treatment. Patients are typically advised to avoid strenuous exercise in the initial stages of treatment. But once their bone pain and lesions are treated, patients may find that low-impact aerobic exercise, and even light weight lifting, can be beneficial.

"Patients are usually feeling better by month three of treatment, and at that point it's good to start some strenuous physical activities," Arora adds. "It's important to maintain some level of physical fitness to prevent fatigue and loss of muscle mass."

Padjen, who is now in remission, agrees. Although he still has some bone pain, and he leans on his service dog, Flynn, to help him with everyday tasks and basic mobility, he feels well enough to walk four miles a day. "I'm feeling really good," Padjen says. "I think the exercise helps tremendously."

> Just put your shoes on. Then once your shoes are on, getting out the door and walking to the mailbox becomes a little easier.
>
> —KENNY CAPPS

Exercising also helps patients maintain a healthy weight, says Dr. Anita D'Souza, associate professor of medicine at Medical College of Wisconsin in Milwaukee. "We often see obesity and sarcopenia, a loss of healthy muscle, in (patients with) multiple myeloma, and there's a concern that these factors may contribute to disease progression," D'Souza says. "Getting to a healthier weight should be a goal for all patients."

D'Souza co-authored a recent study of 38 survivors of multiple myeloma, 76% of whom were obese. Several participants reported significant quality-of-life challenges, including fatigue, pain and a loss of physical function. The results support the need for lifestyle coaching in the treatment of multiple myeloma, she says.

"The majority of patients weren't involved in any exercise programs, but they expressed an interest in it," she explains.

Capps also has found that staying active helps to keep his bone pain under control. In 2020, he ran four marathons, one 50-mile race and 63 miles of a 100-mile race. He managed all of that despite undergoing surgery earlier that year to remove his adrenal glands and a tumor that was sitting on top of one of them.

Now Capps raises awareness of the benefits of exercise in the treatment of blood cancers through his nonprofit organization, Throwing Bones. The organization provides educational videos and coaching for health care providers who want to educate patients with cancer about the benefits of exercise.

Being physically fit "can optimize your quality of life and make you healthy enough to withstand treatments that otherwise you may be ineligible for, like bone marrow transplants," Capps adds.

Capps knows from experience that cancer treatments can cause fatigue, which can sap the motivation to exercise. For patients who are struggling to stay active, he has one piece of advice: "Just put your shoes on," Capps says. "Then once you have your shoes on, getting out the door and walking to the mailbox becomes a little easier. Then maybe next time you can walk around the block. Just get your shoes on and see where that goes."

SOCIOECONOMIC GAPS CAN LEAD TO POORER OUTCOMES IN MULTIPLE MYELOMA

By KATHERINE MALMO

Patients facing financial, demographic or racial disparities may struggle to get the best treatments and access to clinical trials.

HYEJIN KANG / STOCK.ADOBE.COM

In 2021, more than 34,000 Americans received a diagnosis of multiple myeloma, a number that has been fairly consistent over the past 20 years, according to the National Cancer Institute. The good news is that during that time, survival rates have improved.

What's the bad news?

The survival gap among socioeconomic groups has widened.

HOW IS SOCIOECONOMIC DEFINED?

Mark A. Fiala, an instructor at Washington University School of Medicine in St. Louis and a researcher who focuses on access to care and related issues for multiple myeloma and other cancers, says the term "socioeconomic" is poorly defined.

"We all know what socioeconomic status is, but there's not a pure definition of it," Fiala says. "It relates to a person's financial situation and (as an example) their ability to withstand the onslaught that cancer brings, particularly multiple myeloma." »

LYNN MCLEAN
is using money she saved for retirement and raised via a GoFundMe account to pay for just her treatment plan.

Fiala says people who are able to continue treatment may have better insurance with lower deductibles, money in savings, or access to charities and organizations that can help. This is true but only part of the picture. The definition of socioeconomics also goes beyond finances.

According to Dr. Karen Winkfield, executive director of Meharry-Vanderbilt Alliance and the Ingram Professor of Cancer Research at Vanderbilt Ingram Cancer Center in Nashville, Tennessee, the definition of socioeconomic status includes a person's occupation and education.

"We know that socioeconomic status is the greatest driver of health outcomes period," says Winkfield, who also is a radiation oncologist specializing in the treatment of blood cancers. "We know that, but there are also things like physical environment and literacy rates — not just whether a person can read, but also health literacy — that are important."

And when investigating socioeconomic gaps, race shouldn't be overlooked.

Catherine Marinac, an assistant professor of medicine at Harvard Medical School and Dana-Farber Cancer Institute in Boston, is trained as a cancer epidemiologist. Her focus is on factors that influence outcomes in multiple myeloma and other plasma cell disorders. She points out that older and minority patients do not get the same benefit from emerging multiple myeloma therapeutics as younger nonminority patients.

Each of these factors — financial, demographic and racial — plays into multiple myeloma outcomes.

FINANCIAL DISPARITY

Lynn McLean, a family physician on health leave who lives in Calgary, Canada, received a diagnosis of multiple myeloma in November 2021 at age 60. However, securing the right treatment is proving to be a challenge.

"I did not expect to have to make the decision about whether to pay for an upgrade to a different drug protocol that is standard first line of care in the (United States of America) but not in Canada," McLean explains. "The idea of a national standard for treatment sounds good; I just don't agree with the current choice."

McLean believes the treatment plan for patients with multiple myeloma needs to be upgraded. If she has to pay for the four-drug regimen, including Darzalex (daratumumab) and Revlimid (lenalidomide), which is becoming the first line of defense in the U.S., it will cost approximately $140,000 in Canadian dollars (approximately $110,000 in U.S. dollars). She has insurance to help pay some of the bills and is using her retirement savings along with funds donated through her GoFundMe account.

"Without that I'd be destitute," McLean says. "I don't have masses of savings to divert easily to these additional drugs, and my drug plan doesn't pay for them."

According to Fiala, financial toxicity hits patients with multiple myeloma especially hard because unlike most cancers that go through an acute treatment phase that ends, multiple myeloma is a chronic condition that continues from diagnosis to end of life. Furthermore, most patients are older than 70 and many live on fixed incomes that make it difficult to pay for expensive treatments.

In these instances, some doctors, according to Fiala, ask patients how they'll pay for their medications. The challenge, however, is that patients' financial situations can change quickly depending on annual deductibles, maximum out-of-pocket charges, status of their disease, relapses, new tests or treatments, and even everyday life. Sometimes, for instance,

PHOTO PROVIDED BY LYNN MCLEAN

a car needs to be repaired, and the unexpected expense may make it difficult to afford treatment.

"There are copay assistance programs," Fiala says. "But (most) don't solve the problem. It gets a patient access or services, but in a couple months they'll be back in the same situation."

This heavy financial burden can affect treatment.

"People may not be able to take their medications if they have higher copays," Winkfield adds. "Not taking medications regularly is problematic because that may prevent or delay eligibility for a transplant. And we know that those who get transplants following a first complete response have longer remissions than those who don't. All of these things can compound one's ability or inability to take care of themselves. And that obviously is going to impact outcomes."

DIFFERENCE IN DEMOGRAPHICS

In 2003, Joan Rodriguez was a 38-year-old dental hygienist living with her husband and son in Boston when she received a diagnosis of monoclonal gammopathy of undetermined significance (MGUS), which can be a precursor to multiple myeloma. She started treatment at Dana-Farber Cancer Institute, and when she received a diagnosis of full multiple myeloma in 2019, she underwent an autologous stem cell transplant. Now Rodriguez takes Darzalex (daratumumab) and Revlimid (lenalidomide). Since her health coverage includes Medicare Part A (a monthly premium isn't paid if a patient or their spouse has paid Medicare taxes for a certain amount of time while working) and MassHealth (insurance offered to qualifying individuals and families living in Massachusetts with benefits that may directly or help pay for part of health insurance premiums), her medical costs are low. Moreover, Rodriguez benefits from being within close proximity to Dana-Farber.

However, many might not experience this same benefit. Living in a neighborhood with low socioeconomic status is associated with worse rates of multiple myeloma survival, according to a study published in *CA: A Cancer Journal for Clinicians*.

Winkfield points out that multiple myeloma symptoms can be nonspecific and some people who do not have consistent health care may not identify the signs.

"The patient might feel fatigued," Winkfield says. "They might have a little bone pain. And so, if you're not used to being involved in the health care system, if you do not have a primary care provider, you might not notice some of these things. You might not have routine blood work that could show you have anemia or kidney dysfunction."

ASSUMPTIONS ABOUT RACE

According to the American Cancer Society, Black men and women are twice as likely as their White counterparts to develop multiple myeloma. Black women are twice as likely to die of the disease, whereas the number is slightly less for Black men.

The reasons for this are complex.

"Doctors make assumptions about you," Rodriguez adds. "They look at this Black woman with a low income and state's insurance and think: What's going on here? My first doctor tried to make me think my pain was psychological and not physical. I told someone in patient relations that I wanted a different oncologist and they told me I had to stay with him. But I said, 'You're telling me that if I don't see him I can't come to the institute?' Then I got a new doctor."

> The biggest thing is building trust. And this is relationship building. There's no trick to it.
>
> —DR. KAREN WINKFIELD

Rodriguez solved this problem, but the process was intimidating and she found it especially hard to tackle while she was in treatment for cancer. So what are institutions and doctors doing to reduce racial bias and discrimination in the medical system?

"The biggest thing is building trust," Winkfield explains. "And this is relationship building. There's no trick to it. Physicians, institutions, and the medical and health care systems themselves have done so much to disenfranchise individuals. It's now our time to turn around and say: We acknowledge that we've not always been there, but here we are now. What is it that you need? How can we help to build trust? We're tapping into community-based organizations and empowering them to assist with recruitment, retention and, in some clinical trials, access to care in general."

Another reason why Black patients with multiple myeloma don't fare as well is that there are fewer Black patients enrolled in clinical trials.

"The innovation of targeted novel therapeutics enrollment in clinical trials has become supremely important," Marinac says. "Even though minorities make up 20% of (patients with) multiple myeloma in the U.S., their accrual rate in research studies is considerably lower."

Enrollment in clinical trials is important for multiple reasons. First, it's needed so research organizations can gather a diversity of data to study the safety and efficacy of »

PHOTO PROVIDED BY JOAN RODRIGUEZ

> **JOAN RODRIGUEZ** encourages other patients to find someone who will listen and help if they feel something is wrong or they are being mistreated.

new drugs, but also, Marinac points out, trials can provide access to the most innovative cancer therapies that are not yet standard of care, and the drugs are generally paid for by the sponsor of the study.

NOW WHAT?

Winkfield believes the best solution involves rethinking health care in the U.S. "I know it's scary; I know it's hard," Winkfield says. "But do we consider health care a right? Or is it only for a privileged few? And if it is a right then what are the ways we need to redesign our health care systems to make sure it's equitable for everyone, including individuals from rural backgrounds, those who live on (Native American lands) or those who might be in underserved communities?"

Fiala says universal coverage is a good place to start, but also points out that many countries with publicly funded health care still find outcome disparities in patients with multiple myeloma.

"It's been observed in countries like Australia, Sweden and Canada that patients with lower socioeconomic status still do worse," Fiala says. "And these are places where access should be equal based on coverage. But there are things that aren't fully accounted for beyond being able to pay for the treatment. Many multiple myeloma treatments are (given intravenously) and patients come in several times a month and transportation can be a problem. There are a lot of complications that factor into the equation."

These outcome disparities, however, may be opposite within the Veterans Health Administration (VA). In 2019, researchers accessed the VA's national records and identified 15,717 patients with multiple myeloma. At the VA, Black patients with multiple myeloma under age 65 had better survival rates than their White counterparts. For patients over 65, the median survival rate was similar between Black and White patients with multiple myeloma.

"We don't find disparities based on socioeconomic status, by race or by anything along those lines in the VA because it is a 360-degree coverage system," Fiala explains. "If you don't have transportation, they'll send a car for you. It is a more complete program. And that's the only place we don't see these disparities."

In the meantime, Marinac would also like to see outreach efforts expanded so that patients can easily access information on where they can find specialized myeloma treatment centers and clinical trials. Resources such as the Multiple Myeloma Research Foundation, Myeloma Crowd, and the HealthTree Foundation offer some of this information. She also says that continued use of telemedicine beyond the COVID-19 pandemic may help provide some solutions for reaching rural and underserved communities.

Rodriguez wants to give patients with multiple myeloma a message of hope and encouragement.

"You just have to keep advocating for yourself," Rodriguez says. "You have to value yourself. If you feel you're not being treated well, if you have a question or this doesn't feel right, or if you're being mistreated, you have the right to go and get someone else to help you and listen to you."

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HOW DOES MULTIPLE MYELOMA AFFECT COVID-19 VACCINES?

When cancer harms the body's ability to make antibodies, what does that mean for vaccines?

By SONYA COLLINS

In December 2020, Ryan Johnson, a 49-year-old emergency room physician assistant in Roanoke, Texas, received a diagnosis of multiple myeloma. He was grateful that at least he had already gotten his first dose of Pfizer's COVID-19 vaccine.

A cancer of immune system antibody-producing cells called plasma cells, multiple myeloma has been shown to make people more vulnerable to COVID-19 infection and serious complications. Johnson already faced plenty of risk working in an emergency room. In people with multiple myeloma who are not vaccinated, COVID-19 causes moderate to severe acute respiratory dysfunction in more than 75% of those infected. And according to a 2021 study published in *JAMA Oncology*, approximately one-third of people with multiple myeloma who go to the hospital for COVID-19 will die.

Shortly after completing induction treatment for multiple myeloma, Johnson was due for his second shot. A few weeks later, he was fully vaccinated by the Centers for Disease Control and Prevention (CDC) standards at the time. His hematologist-oncologist tested Johnson's blood to measure his response to the vaccine. »

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RYAN JOHNSON wasn't completely surprised after he found out that he mounted no response after his first two COVID-19 vaccines.

JARED REY HERNANDEZ

"I had mounted no response at all after the first two shots," Johnson says. "I was a little disappointed, but I wasn't surprised."

Not only does multiple myeloma make people more susceptible to contracting COVID-19 and having complications from it, it also limits the immune system's response to the vaccine. These are consequences of both multiple myeloma's effect on antibody-making plasma cells and of immune-suppressing treatments for the disease.

"People with multiple myeloma have more prolonged infections and higher risk of complications from those infections, and we know that vaccines work far less well for them," says Dr. Amrita Krishnan, director of the Judy and Bernard Briskin Center for Multiple Myeloma Research at City of Hope in Duarte, California.

However, additional vaccine doses may help. For people with immune-compromising conditions, including multiple myeloma, the CDC now recommends three initial doses of an mRNA vaccine (that is, Pfizer or Moderna) spaced 28 days apart followed by a fourth dose as a booster five months after the third shot. For people with immune-compromising conditions who receive the Johnson & Johnson single shot, the CDC recommends a booster with any of the three available vaccines two months later. New and experimental treatments with emergency use authorization from the Food and Drug Administration (FDA) may soon provide immune-compromised people with antibodies in a way that vaccines cannot. Doctors recommend that people with multiple myeloma also continue to take basic precautions such as appropriate masking and physical distancing.

THE ADDED RISK

Antibodies are the body's natural defense against illness, and when viruses or bacteria enter the body, the immune system typically recognizes them as a threat. Healthy plasma cells in the bone marrow then manufacture proteins called antibodies, which are custom-designed to fight off that specific invader. For every infection, the immune system makes a corresponding antibody to fight it.

Similar to germs, vaccines also trigger the production of antibodies when they enter the body. Typically, the vaccines deliver just a bit of deadened virus — or a type of material like cellular tissue that behaves like the virus in some way — into the bloodstream so that immune cells will detect it and begin to manufacture the appropriate proteins to fight it. That way, if the actual virus ever gets into the body, the immune system will have the tools to fight back. With mRNA viruses, like COVID-19, however, the mRNA vaccines guide patients' cellular tissue to produce the viral protein to best trigger the immune system in part, not the whole virus.

> I had mounted no response at all after the first two shots. I was a little disappointed but not surprised.
>
> —RYAN JOHNSON

"Individuals who have multiple myeloma or its precursor condition, smoldering myeloma, have a compromised immune system. That's why, even before COVID-19, they had a higher risk of acquiring infections. And now they have a higher risk of (contracting) COVID-19, too," says Dr. Ankit Kansagra, a hematologist-oncologist at UT Southwestern Medical Center in Dallas.

Because multiple myeloma is a cancer of antibody-making plasma cells, the disease affects the body's ability to produce effective antibodies. The cancerous cells instead make defective antibodies that the body cannot use and that can harm the body.

Multiple myeloma treatments, which suppress the immune system, can also make people more susceptible to infections, Kansagra adds. "Also, we know that multiple »

» **RYAN JOHNSON** says he had a "great response" after receiving a third vaccine.

JARED REY HERNANDEZ

myeloma is typically a disease of (older patients), and research on COVID-19 suggests that the older the person (is) the greater the likelihood of serious complications." Finally, he notes, "multiple myeloma compromises organ function, which can lead to further issues with COVID-19. All these things together make people with multiple myeloma more prone to severe infection."

MULTIPLE MYELOMA AND COVID-19 VACCINES

Results of a July 2021 study published in *Nature* found that only 45% of people with active multiple myeloma who received one of the mRNA vaccines had an adequate response. Some (22%) had a partial response, and the others had no response at all. Response rates were higher in people with smoldering disease. Results of large studies published in *JAMA Oncology* show that fewer than 1% of people with multiple myeloma who are vaccinated received the Johnson & Johnson vaccine, so most efficacy data refer to the mRNA vaccines.

Multiple myeloma treatments affect vaccine responses as well. Results of a July 2021 study in *British Journal of Hematology* found that people who had already been treated with four or more drugs for multiple myeloma were less likely to have an adequate response to an mRNA vaccine. Those receiving anti-CD38 therapy, such as Darzalex (daratumumab), or anti-B-cell maturation agents, such as CAR-T cells or bispecific T cell engager therapy, seem to have the poorest response to COVID-19 vaccines.

The good news is that additional doses of the vaccine may trigger the desired immune response in some immune-compromised people.

When Johnson received a third dose as a booster last August, he says, "I (had) a great response at that point. I developed antibodies and everything."

The added protection didn't come a moment too soon. By that point, the pandemic had been raging for more than 18 months. Johnson, who had been living with multiple myeloma for nearly a year, had returned to work, where he was seeing at least six or seven patients with COVID-19 each day. And home was no safer. Johnson's wife, a nurse, contracted the virus, and so did their two sons.

VALERIE TRAYNHAM did extensive research before receiving her doses of the vaccine.

By taking precautions at work and sleeping in a separate bedroom and wearing a mask at home, Johnson managed to avoid infection.

"Somehow, miraculously, I did not catch it," he says. "I was getting swabs, just to see if I needed to get the monoclonal antibodies if I ended up catching it, but it never developed."

Stem cell transplant, a common treatment for multiple myeloma, also may interfere with vaccines. In fact, it can wipe out all the antibodies developed from a lifetime of vaccines, including COVID-19 vaccines. Generally, doctors recommend that people get all the necessary vaccines for their age again after recovery from a stem cell transplant.

Johnson's COVID-19 antibody levels remained sufficient after his recent stem cell transplant. His doctors will continue to monitor his levels before administering another shot.

DOING RESEARCH, MOVING ON

Valarie Traynham, who has breast cancer and multiple myeloma, plans to get all four recommended doses of the Pfizer vaccine So far, she's had three. She did a lot of research even before the vaccine was available to the public.

Many of Traynham's friends and family didn't initially plan to get the shot. They had been swayed by misinformation, and Traynham wondered if some of their concerns might be true. She also wondered just how much the vaccine would benefit someone in her condition.

"I already have a suppressed immune system, so is this vaccine even going to help me? That was the one question that I kept asking myself," says the 49-year-old, who leads the African American Multiple Myeloma Chapter for the HealthTree Foundation and lives in Aurora, Illinois.

A talk given by Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, at the American Society of Hematology's annual meeting in December 2020 made up Traynham's mind.

PHOTO PROVIDED BY TRAYNHAM

> I encourage all my patients with multiple myeloma and their families to get the vaccine because we know that COVID-19 mortality is much worse in people with multiple myeloma.
>
> —DR. AMRITA KRISHNAN

"That was one of the questions that (patients with blood cancer) had for him, and he said, 'Having some type of protection is better than nothing at all,'" Traynham says. "When I heard that, I thought, I can't just live this sheltered life forever. My friends were going to get the vaccine and move on with their lives and I was going to be stuck wondering 'What if?'"

After Traynham received her first dose of the Pfizer vaccine, she enrolled in a study with the Leukemia & Lymphoma Society to measure vaccine responses in people with blood cancers. Tests revealed that her immune system had produced very few antibodies after the first shot, but after the third, she had produced substantially more.

"It was better, but still not nearly what you would see in a person who doesn't have multiple myeloma," Traynham says.

NEW TREATMENT AND PREVENTION FOR COVID-19

For those who don't have a sufficient response to a COVID-19 vaccine, new and experimental treatments may help stave off severe infection.

The FDA has granted emergency use authorization to three different monoclonal antibody therapies for people who test positive for COVID-19, have mild to moderate symptoms and run a high risk of developing severe disease, which includes people with multiple myeloma. The therapies are bamlanivimab plus etesevimab, REGEN-COV (casirivimab plus imdevimab) and Xevudy (sotrovimab).

Monoclonal antibodies are laboratory-manufactured antibodies custom-made to fight a specific illness. Unfortunately, only Xevudy has shown to be effective against the omicron variant of COVID-19.

"The goal is to get them the treatment as soon as possible after infection so that we're able to prevent that infection from becoming severe," says Dr. Shagun Arora, a hematologist at UCSF Health in San Francisco.

Two of the monoclonal antibody treatments, bamlanivimab plus etesevimab and REGEN-COV, also have emergency use authorization as post-exposure prophylaxis. This means that people who have been exposed to someone infected with COVID-19 and who run a high risk of severe disease if they get infected themselves can receive one of these treatments as soon as they are exposed — even before testing positive for the virus. But these are also not effective against the omicron variant.

More recently, the FDA approved Evusheld (a combination of the two monoclonal antibodies tixagevimab and cilgavimab) for use as preexposure prophylaxis in people who have moderate to severely compromised immune systems and who may not have a response to a COVID-19 vaccine.

"This is a game-changer in the minds of many doctors who treat immunocompromised patients," Arora says.

Last December, the FDA approved two oral antiviral medications, Paxlovid and molnupiravir, for people who test positive for COVID-19 and run a high risk of hospitalization, death or other complications.

CONTINUED VIGILANCE

As breakthrough infections of COVID-19 continue to occur in vaccinated people both with and without multiple myeloma, doctors recommend that people with this type of blood cancer take all precautions available to them and continue to be vigilant against infection.

"I encourage all my patients with multiple myeloma and their families to get the vaccine because we know that COVID-19 mortality is much worse in people with multiple myeloma," Krishnan says. "But beyond that, you still need to treat yourself as if you're high risk. Continue masking, avoiding large gatherings and (being) extremely cautious."

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SCAN THE QR CODE to hear more about **JOHNSON**'s journey with the COVID-19 vaccine and multiple myeloma.

Collaboration Through Communication

As part of its "Speaking Out" video series, *CURE*® spoke with Throwing Bones founder Kenny Capps about the importance of patient-physician communication during a myeloma journey.

By KRISTIE L. KAHL

WITH A VARIETY OF treatment options available across the different stages of multiple myeloma, it is vital for patients to not only work collaboratively with their care teams to determine which option is best for them, but to also seek such care from a group of disease specialists.

Through the mission of raising awareness, promoting education and inspiring others through fitness and health to combat blood cancers, Throwing Bones aims to help patients with myeloma navigate their journey with the disease. Founder and executive director Kenny Capps sat down with *CURE*® to explain the importance of patient-physician communication, how patients can be their own best advocates and why seeking a myeloma specialist is important.

Q: Can you explain why patient-physician communication is key when it comes to a patient's journey with myeloma?

A: One of the biggest challenges that health care providers in general, but certainly your diagnosing oncologist, have is being able to understand exactly what the patient is going through. Sure, they can do blood work, they can do different types of scans, they can check you out from stem to stern. But sometimes it's hard to know exactly what's going on unless you're able to verbalize it.

And I understand that as a patient, sometimes it's difficult to understand what's going on. But at least, if you can communicate how you're feeling and what's happening in that moment, they can make decisions that actually better serve you. And then it introduces treatment options (or) caring for you in a different way. Maybe it's leading you to a different health care provider in order to handle some of those symptoms or the responses to the current treatment.

Q: How does this collaboration play a role in patients being their own best advocate when it comes to their care and their treatment decisions?

A: You really need to be invested fully in yourself. And that's tough, because it's an overwhelming experience in a lot of ways. For one thing, it's new. And the other thing is that it's a really serious topic. It's something where it's life changing in a lot of ways, and so that information is tough to actually take in all at once; however, you are the one who is best suited to communicate with others, even if it's just to your caregiver, what's going on with you. Which means that you need to basically understand the premise of your disease, what it is that you have, what could be showing up, and also, at least in a very general way, what options are available to you. But you have to be your own advocate in order to do that.

Q: As a part of this communication, why is it key for a patient with myeloma to make sure that they're seeing a myeloma specialist?

A: Myeloma is an interesting blood cancer, because there hasn't been (historically) as much research over the past, say, two, three decades. Within the past 10 years, the amount of changes that has happened within the myeloma landscape has been phenomenal. And so, it changes quickly.

And although more and more people are becoming aware of (myeloma), it still isn't as common as some of the cancers that most of us are familiar with, say, you know, breast cancer or prostate cancer, (diseases) that typically are more common. And so there's not as much need to have a specialist in every community (with the more common cancers). Which means that there are lots of oncologists probably in your community or near your medical center that focus on blood cancers, but not necessarily specific to myeloma. So they're not aware of the latest updates and trends that we're heading towards, the things that are necessary in order to get you to your next best place. And so having a specialist, someone who focuses solely on multiple myeloma, I believe is essential to the right treatment for almost every patient.

cure® EDUCATED PATIENT® SUMMIT

EVENTS THAT EDUCATE AND INSPIRE

CURE® hosts Educated Patient® Summits virtually throughout the year. We invite expert physicians and advocates to share the latest information regarding a cancer diagnosis, treatment options, clinical trials, genomics, survivorship, and long-term effects. We invite you to be a part of the half-day summits to learn and empower your healing journey.

Summits are held on Saturdays at 11am ET | 8am PT

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- **Skin Cancer** – June 18

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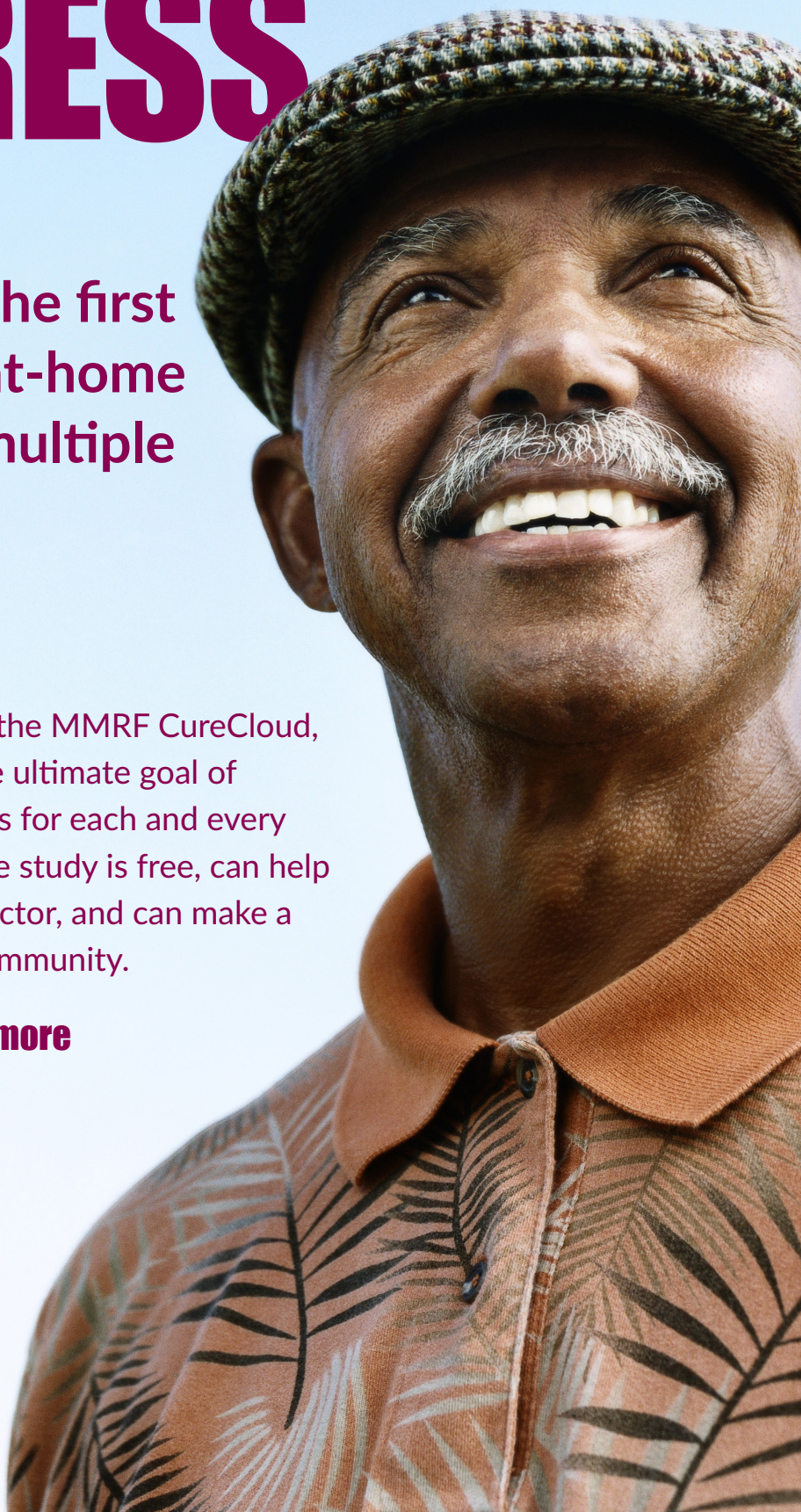

Our groundbreaking research study, the MMRF CureCloud, will help accelerate research with the ultimate goal of identifying smarter treatment options for each and every multiple myeloma patient. Joining the study is free, can help inform your discussions with your doctor, and can make a difference for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

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