

FAQs on Treatments, Monitoring, and Maintenance for Newly Diagnosed Multiple Myeloma Patients

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Transcript

Mary DeRome (MMRF): Welcome everyone, and thank you for joining us for today's session. I'm Mary DeRome, Senior Director of Medical Communications and Education at the Multiple Myeloma Research Foundation. Today I am joined by Dr. Sergio Giralt and Ms. Emily Patterson from the Memorial Sloan Kettering Cancer Center in New York City, and Richard Knox, a patient from Charlottesville, Virginia.

We've invited them here today to answer frequently asked questions about initial treatments, maintenance therapy, and monitoring for newly diagnosed multiple myeloma.

Let's start with questions about induction therapy and whether myeloma stage matters with respect to treatment choices. Dr. Giralt, for a patient who's just been diagnosed, how do you and the patient decide on the best course of treatment, and does being stage 1, 2, or 3 factor into that decision?

Sergio Giralt, MD: Myeloma staging is actually very interesting. Myeloma is a blood cancer, so it's not like breast cancer where it's staged by size and if you have lymph nodes involved. Myeloma is staged with what we call the International Staging System (ISS), in which we measure albumin, which is a protein that we have in the blood and beta-2 microglobulin, which is also a protein that's established on myeloma cells. If your beta-2 microglobulin is very high, more than five, you're stage 3.

Now there's also the revised ISS, in which we incorporate chromosome abnormalities. There are a variety of chromosome abnormalities that we call high-risk cytogenetic abnormalities; these include del(17p), t(4;14), and t(14;16). The presence of these chromosome abnormalities in the myeloma cells predicts a worse outcome.

Does it make a difference? Well, it depends on how a patient presents. A patient who presents with renal failure is actually a medical emergency that requires admission, plasma exchange, and hydration, so that we can preserve and save kidney function. A patient who presents with a cord compression because of plasmacytoma is a medical emergency.

The most common presentation in the United States today is a patient who presents with fatigue, bone pain, or serendipitously was getting their yearly

physical examination, was found anemic with an elevated total protein, and was at that time referred.

The first thing one does after making sure that there's no emergency is to stage that patient, which involves the bloodwork, a bone marrow biopsy, and total-body imaging—total-body PET, CT, or MRI.

Then, with that piece of information, the hematologist, oncologist, and myeloma specialist sit down with the patient. Each patient is an individual. And, depending on their performance status and their age, they devise what we call the induction therapy. Patients with stage 3 disease are patients at high risk. They behave differently than patients with stage 1 and 2 disease. Actually, some patients with stage 1 disease, many times we don't treat them: they fall into that category of smoldering or asymptomatic. They have no symptoms. We might watch them for a period of time, because we don't know whether they really have active myeloma or their myeloma isn't moving and isn't causing them any problems. Patients with stage 2 disease usually all have to be treated. We recognize that four-drug induction is better than three-drug induction. Four-drug induction involves more treatment and sometimes more side effects. But if you have stage 3 disease, it makes a dramatic difference. Currently, I think we are moving more towards four-drug inductions for everything, because the results of the GRIFFIN trial and the CASSIOPEIA trial are fairly dramatic.

Mary DeRome (MMRF): Emily, it seems like all treatment options offered to patients when they're newly diagnosed have dexamethasone as one of the drugs in the regimen, and it is often poorly tolerated by patients. I'm sure that you hear about that a lot. Can you tell us why it's used and whether there are ways patients who have to be on it can tolerate it better?

Emily Patterson, NP: You're correct: dexamethasone is often used as part of induction therapy, and it is one of the three or one of the four drugs used in triplet or quadruplet combination therapies.

The primary reason is that it enhances the potency of the drugs it is used with, Revlimid or lenalidomide being two examples of that. It is also used to combat the side effects of treatment, such as nausea or allergic reactions that we can see with something like daratumumab or even rashes with lenalidomide.

But to tolerate steroids or dexamethasone, in particular, better, we do recommend taking it first thing in the morning and with food to minimize issues related to insomnia or GI upset. It should be taken with an antacid and over-the-counter drugs like omeprazole—that is, Nexium or Prilosec—to protect the stomach.

For more serious complications from dexamethasone—such as high blood sugar, high blood pressure, or mood disturbances—dose reduction is often recommended. In more severe cases, the drug can be stopped.

Mary DeRome (MMRF): Rich, can you tell us how you were diagnosed with myeloma, what initial treatment you received, and how you decided on that treatment?

Richard Knox: Flashback to December of 2011. I am a minister, and advent is an extremely busy time right before Christmas. I was limping along and I had to tell people in church, “Don’t tell Nan, my wife, that I’m limping or anything like that.” But I was limping. It was midweek, at the end of a long day.

I went down to where the church had a tutoring program, and one of the high school tutors was done. Her mother was a colleague of mine in a different church, and I needed to talk to her. I said, “Rachel, I’ll walk you out to your car.” I walked out with her and I hear a buzz, the window comes down, and lo and behold, it’s not her mother, but her father—who happened to be my primary care physician.

He said, “You’re limping. Come into my office next week.” In other words, immediately after Christmas. So I did. He sent me to a physiologist, who said, “Oh yeah, this is pretty much arthritis. We’ll just do a quick x-ray and go from there.”

On Christmas Eve, twins I had baptized a year and a half earlier came to the children’s Christmas Eve program. I always try to see people eye to eye, so I bent down, and I had sharp pain right here in my chest. That’s the only pain I ever had with my experience of multiple myeloma, except for the bone marrow transplants.

Sergio Giralt, MD: The bone marrow harvest.

Richard Knox: As Dr. Giralt likes to say, “Here comes the woodpecker.” The physiologist called back after a couple of days and said I needed to have an MRI. My antennas went up; I said, “I will come and pick up the ‘script and take it to the MRI office.” I took it in and said, “I’m not leaving here until I’ve had this.” They thought I was joking. I just sat down. lo and behold, within a half hour, they had me out of there. But then the physiologist calls and said, “Tom’s just expecting a call from you. Give him a call.” I called, and Tom said that it looked like it was myeloma, but they weren’t sure.

He said, “Come in for an appointment.” At the appointment, he asked if I wanted a second opinion from Memorial Sloan Kettering. That was a no-brainer. He put me the local hospital for a whole bunch of tests and so I wouldn’t be walking on my leg. I went in, and Dr. John Healey, who was the orthopedic oncologist I

interviewed with initially, kept saying, “Yes, yes, good, yes, yes” the entire time. Then he said, “This is what we’re going to do. I’m going to admit you to the hospital right now, and I’m going to operate tomorrow.” He replaced my left femur. Apparently, I had shattered it from the inside out.

I was in the hospital a long time for that. I was in traction for an extended time. That pain I felt on Christmas Eve was a tumor that was up against my spinal cord. My understanding is that they would normally do surgery, then chemo, then radiation. But they felt they had to do radiation right away.

We started at the end of my time in the hospital. I was learning how to walk again, with a walker, crutches, a cane. We did 15 sessions of that. Then we started with the Velcade, dexamethasone, and Revlimid for me just to knock the myeloma down as much as we could until it got to a good level.

Then we stopped a while for my bones and my body to rest. Then we harvested my stem cells, then two days and a decade ago I started my transplant. My day zero was June 27th of 2012. That’s how we got into it.

Sergio Giralt, MD: Ten years ago, which is really great and he’s very active, has grandchildren. For those of you out there, it is incredible. Things have changed a lot in the myeloma field and induction.

The transplant component, I guess we still use melphalan at high doses. Many centers are now doing outpatient transplants, which is a change. For many patients, outpatient transplant is really a game changer, because it allows them to live in a homebound environment.

Actually, Duke and Memorial now are doing a study on homebound transplantation, where patients actually stay at their home or in a homelike environment, and the nurse practitioners and the medical team go to them. With telemedicine now, many of these things are much more feasible. We are studying ways that we can make transplant much easier, with less toxicity.

Mary DeRome (MMRF): Let’s talk about bones and bone lesions. When somebody replaces your femur, what do they put there instead?

Richard Knox: It’s a titanium rod. When Dr. Healey was putting it in, he said the only pristine—talking about bone lesions—part of my bone structures was my left socket. That’s still me, that’s mine, but the femur itself and the ball is his. Right now, occasionally, I have of arthritis there, but it’s a good trade-off.

Mary DeRome (MMRF): Many patients have bone lesions at the time of diagnosis. Dr. Giralt, does induction therapy help the bone lesions to heal, or do you have to give other treatments? What’s the best way to deal with this bone pain and bone lesions?

Sergio Giralt, MD: it's interesting that Rich described this as his femur shattered from inside out, because what happens, as the myeloma grows, it destroys first the inner part of the bone, what we call the bone stroma, then destroys the walls and creates a larger cavity. Eventually it starts growing and it starts eroding the cortex. The cortex is that hard part of the bone, the thing that gives it its strength.

As the myeloma grows, it breaks the cortex. You can also imagine that it weakens the cortex. A common story with myeloma patients is, "I lifted my granddaughter and suddenly my humerus cracked." Or, "I was lifting a shopping bag and I fell and I cracked a hip." These are called pathological fractures. In many cases, when we do that total body imaging, one of the things we're looking for is what we call lytic lesions. These are the holes that the myeloma causes as it grows locally. If a lytic lesion is actually eroding the cortex of a weight-bearing bone—weight-bearing bones being your lower and your upper extremities—or if they're eroding your vertebral bodies, there's a risk for a compression fracture. These patients are what we call prophylactically irradiated, or, in Rich's case, if he had discovered this before he fractured, he would've been prophylactically taken to surgery and had a metal rod put in to avoid a pathologic fracture.

What happens if a patient doesn't have those? Does that mean that their bones are healthy? No. By definition, all myeloma patients have a proclivity for fractures. We test bone density at baseline, but treatment can, even if your bone density is normal, cause loss of bone. These patients get what we call bone-strengthening medicines. There are two types: one is the bisphosphonates. There are two available: pamidronate and zoledronic acid.

The one that's most commonly used is zoledronic acid, because it can be infused over half an hour to an hour. Pamidronate requires 90 minutes to 2 hours. The other bone-strengthening treatment is a monoclonal antibody called denosumab, trade name is Xgeva.

These are equivalent. They're very good in reducing the risk of what we call skeletal-related events or pathologic fractures. In addition to that, patients should be taking vitamin D, which is essential for bone health, and on certain occasion calcium supplementation.

Mary DeRome (MMRF): Emily, tell us about these bone-strengthening treatments, Zometa and Xgeva. How are they incorporated into the treatment schedule? How often do patients have to come into the clinic to get them, and how long are these types of treatments given for?

Emily Patterson, NP: Carrying over on what Dr. Giralt said, Zometa, Xgeva, and pamidronate are often started at the same time as induction therapy. And, like Dr. Giralt said, these can be given as either treatment or prevention of bone destruction from myeloma, and also from the treatment itself—that is, from

dexamethasone or steroids. We will start with a skeletal survey or a DEXA scan, which assesses the bone density, prior to initiating therapy or around the same time, just to see where are we starting with the bones.

Do we have normal bone density? Are we in-between with osteopenia or do we have osteoporosis? Generally, we recommend starting treatment every 3 months, regardless of what that bone density scan shows for a 2-year period, and then reassessing with another DEXA scan, re-imaging the bone strength and dosing further based on those results.

if your bone density got worse, maybe we continue every 3 months versus; if it got better, we could space it out to every six months, maybe even yearly. You also have to base it on what your myeloma is doing. Are you having more bony lesions? Are the bony lesions stable, or do you not have bony lesions at all?

We can administer the medication on the same day somebody's coming in to get myeloma treatment, just to minimize clinic visits. But some people don't want to have such a long day if they're getting a lot of infusions; they don't have to be the same day. You can spread them out. It's really just patient preference in that regard.

Sergio Giralt, MD: Some physicians give it monthly, which is the way they were approved. We do every 3 months. There is data to show that it's as effective, and it's obviously less treatment burden for the patient.

Mary DeRome (MMRF): Rich, you had your limp, then you had your femur replaced by a titanium rod. Was that the only part of your bones that was affected by your myeloma? Did you take some of these bone-strengthening agents? How were they for you? Did you have side effects from them?

Richard Knox: We call it multiple myeloma, meaning it was a lot of places, but obviously the most critical initially was my femur, but that pain may very well have been a broken rib. My recollection is that the signs of skeletal myeloma that I had were on my left side. We'd like to remember that my bones were—past tense—like lace. I had lytic lesions. My pelvis was affected, probably, and then my femur. I was treated and I'm still being treated with Zometa. Initially, I was almost monthly with Zometa.

Sergio Giralt, MD: In the beginning, because you had so much. Then we spaced it out to every 3 months.

Richard Knox: It's still going on, but it's once a year. I did take, and I still take, the calcium supplement, vitamin D, and a regular old men's Centrum male multivitamin. But my bones now are in fairly good shape, I think.

Sergio Giralt, MD: Your bone density has increased significantly. There is a question of whether we can stop Zometa, which we have stopped in patients whose bone density returns to normal, because you're only on maintenance lenalidomide; you're not on dex or steroids.

What's interesting is that the number of 10-year survivors for myeloma is increasing significantly. Hopefully many, many more people will be like Rich, where myeloma is something they just manage with maintenance treatment. How can we make sure that Rich gets to his 80s and his 90s in the healthiest way? There is a whole program about long-term survivorship for myeloma. Rich has his skin exam once a year, his dental exam once a year, there's a bunch of surveillance that we have to do, and he stays up with his vaccinations, which is very important.

Richard Knox: I see my dermatologist twice a year and the dentist three times a year. That's to keep watch.

Mary DeRome (MMRF): Let's talk about diagnosed patients getting COVID vaccines and boosters, and the timing of those things. What are the current recommendations?

Sergio Giralt, MD: We follow the guidelines of the CDC. We're telling patients, as soon as they're diagnosed, to get their shots. They should have three booster shots. We monitor the COVID spike. A patient who doesn't develop COVID spike, we give them the long-acting monoclonal antibody to keep them protected.

As important as the vaccination is, it's also important to maintain social distancing and use a mask. If you're immunocompromised, you should not be exposing yourself to risk. There's still a lot of COVID out there. Yes, the current variant seems to be less virulent than the original one and Omicron, but it's more contagious; people can still get really sick.

We unfortunately have lost patients to this variant of COVID. My recommendation to all myeloma patients is get vaccinated, get boosted, get re-boosted, and monitor your titers. Also very important: social distancing, mask wearing, a lot of hand washing, and avoiding people who are sick.

There's still a substantial proportion of persons out there who are not vaccinated. We're also seeing COVID amongst patients who are vaccinated. It's generally very mild: they quarantine for 7 days, then they go back to their lives. We tell them all, call as soon as you know you're positive, and we'll prescribe Paxlovid.

Mary DeRome (MMRF): Emily, we're going to switch gears and talk about patients who have progressed to active myeloma from smoldering myeloma. What is smoldering myeloma and are there treatments for it? For patients who

had smoldering myeloma that become active, are treatments the same as for somebody who hadn't been diagnosed previously with smoldering myeloma?

Emily Patterson, NP: I'm going to have Dr. Giralt help with this question, because I often see patients posttransplant.

Generally, patients who progress from smoldering myeloma to active myeloma receive the exact same treatments as somebody who was diagnosed with active myeloma from the beginning. They would receive the same triplet or quadruplet therapy.

There are treatments for smoldering myeloma, daratumumab being one of them, that are being studied. Yes, we can initiate treatment. It's a discussion of whether it's appropriate, whether the patient is symptomatic, how much the disease is affecting their life. But I'm going to defer to Dr. Giralt for more information.

Sergio Giralt, MD: Smoldering myeloma is a moving target. When I started in the field 30 years ago, you had to have hypercalcemia, renal failure, anemia, or bone lesions to be treated. Those were the famous CRAB criteria. Then the group at Mayo and the group in Spain started seeing that there were many patients who were coming in "asymptomatic," or without CRAB criteria. Within 2 years, their first manifestation of disease was either renal failure or a fracture. You can imagine how painful it is for a physician who's been monitoring a patient for 2 years to have that patient come in and say, "Maybe I should have done something earlier."

They initially identified these criteria: active myeloma, free light chains, ratio greater than 100, bone lesions or lytic lesions seen on total body MRI or pet CT, and bone marrow plasmacytosis of more than 60%. Those patients no longer have asymptomatic myeloma: they have active myeloma, and they need to be treated.

Moving forward, this is a continuum. Particularly with the use of all the lab tests we have, we don't know if a patient has smoldering myeloma or if we simply caught myeloma early. The first step with a patient with newly diagnosed myeloma—who has no CRAB criteria, who has less than 60% plasma cells, and who has no criteria of active myeloma—is to monitor him or her carefully in the initial couple of months. Once a month, once every other month—to get a feeling of whether this is myeloma caught early or a smoldering myeloma.

Once the patient has shown stability for a couple of months, there is what we call high-risk smoldering myeloma, involving a variety of criteria. There are people who have between 20% and 55% plasma cells in their bone marrow. There are people who have very low immunoglobulins. These people, based on large data sets, are predicted to progress to multiple myeloma within the first 2 to 3 years.

What did the Spanish do? They said, “Why are we going to wait? Let’s put them on lenalidomide.” They did a randomized trial: half on lenalidomide, half on observation. The people on lenalidomide, as one would expect, progressed a lot slower because they’re on active treatment. But the surprise to everybody is that they actually lived longer.

The ECOG group did a similar study, which again showed a progression-free survival benefit, but still no survival benefit.

One of the things we need to remember when we start treating smoldering myeloma is that everybody gets the side effects of treatment. If you’re being watched carefully, the years that you’re watched without treatment are years that you gained without any side effects. If you get treated with Revlimid and you have diarrhea and rash for 10 years—I mean, I have patients with smoldering myeloma who would’ve been quantified as high risk, who haven’t progressed. Today, we’re saying that if you have a patient who’s had smoldering myeloma for 10 years, don’t do anything.

Dr. Chari from Mount Sinai makes a great point that the criteria for smoldering shouldn’t be a picture. It should be a movie. It should be assessments over a short period of time, 3 to 6 months, to see whether the patient actually has a disease that seems to be stable and unmoving or slowly growing. Is that paraprotein peak going up? Is that light chain going up? Those are two different entities, and those patients need to be treated early.

Mary DeRome (MMRF): We’re going to switch gears and talk about autologous stem cell transplantations. Dr. Giralt, how old is too old to get a stem cell transplant?

Sergio Giralt, MD: Age is no longer a criterion. What we do consider is whether a patient is fit or not fit, and what other comorbidities he or she has. You have a myeloma patient who’s 85 years old, is totally fit, independent in all activities of daily living, particularly if it’s an ISS stage three, in which even quadruple therapy means that remission is going to last a short period of time, we would consider that patient a candidate for transplant. Now transplant is a choice. It’s a choice patients make based on the recommendations we give them.

You asked, when would you not collect cells?

I collect cells in very few patients over 85. Unless you have really bad myeloma, your life expectancy is probably 10 years, and that’s more or less the life expectancy of a myeloma patient now, and it’s even more. It’s not that age is an absolute barrier, but we do incorporate age in our decision about whether or not we recommend transplant. Really, up to the age of 85, we routinely consider all patients as long as they’re fit and independent in their activities of daily living.

Mary DeRome (MMRF): Emily, can you walk us through how patients might prepare for a stem cell transplant and what their caregivers should prepare for before and after the transplant?

Emily Patterson, NP: The biggest thing for both patients and caregivers is to ask questions. Ask questions of the provider, ask what to expect.

Some questions I can think of are, what is collection like? What do I have to do to have my stem cells collected? What do I experience if I take Neupogen, which is a growth factor to help collect stem cells? What is the conditioning regimen? What are the side effects of the chemotherapy? “Conditioning regimen” meaning the chemotherapy given prior to the transplant. What is the expected course? How long will I have these side effects?

What are you monitoring while I’m in the hospital or out of the hospital? Are you checking my blood daily? What does the bloodwork mean? Will I need blood transfusions? Will I be inpatient or outpatient? Why is one better for me than the other? What is the recovery like, and what things should I be looking out for? Is nausea normal? Is diarrhea normal? Are fevers normal? What should I alert you to? Which is generally everything. We want to know everything.

For caregivers, similar things. Educate yourself about potential side effects and what is normal. Meaning, okay, maybe my spouse, parent, brother, or sister has some nausea—what is too much nausea, such that it needs to be taken care of immediately? Fevers are considered an emergency. Also, help with food preparation. What kind of foods is the patient able to eat?

Also, assisting with medication management at home is really important, because it can become overwhelming, the number of medications, what are they for, and the frequency. A lot of these medications are critical in terms of preventing infection and shouldn’t be skipped.

Some patients find it beneficial to speak to another patient around the same age bracket that they are in. Maybe the same disease. What was their induction like, and what are we doing to proceed to transplant? This can be helpful for some people to have this conversation with another person, but it can also *not* be helpful when it increases the patient’s anxiety. Asking your provider if this is something that would help or hinder my mental and emotional preparation for the transplant.

Mary DeRome (MMRF): Rich, you mentioned that you opted to have a stem cell transplant. Can you talk about that decision? Was it hard?

Richard Knox: Ten years ago, it was clear to me that the gold standard was stem cell transplant. The question for me wasn’t whether to do a stem cell

transplant, it was what type. I had to make the decision between donor stem cell or autologous. We decided that autologous was the way for me.

Regarding what Emily was saying about caregivers: my wife has, for longer than 10 years, been what got me through stuff. There was a point where she had to learn to give me the Neupogen. In fact, it had to be within an hour of giving the stem cells—in New York traffic, and I would be late coming in from New Jersey. I stayed at Hope Lodge and would get the shot. Nan was practicing it, and they were saying, “Good, great, perfect. Next time do it and keep your eyes open.” Then for 4 days we harvested, and we got the number of stem cells that Dr. Giralt wanted. Then we rested, and then we came in to get them back. But the decision about stem cell or not was different 10 years ago than it is now.

Mary DeRome (MMRF): I think that most people do. There aren’t many allotransplants done. Dr. Giralt, you’re one of the few proponents of those.

Sergio Giralt, MD: I think allo transplant is a valid alternative for patients with high-risk disease, particularly if they’re young. If you’re 37 years old, your life expectancy should be about 50 years. Myeloma’s going to cut that significantly. There is data emerging from long-term follow-up of both the American and the European studies. The patients with high-risk myeloma, particularly young patients, had longer remissions and actually better survival if they had an allo transplant up front.

The other place where we think allo should be explored, primarily in clinical trials, is in patients who are multiply relapsed or who relapse early after primary therapy, particularly if they’re young, because these myelomas have a very poor prognosis.

What Rich is said is true. Ten years ago, we didn’t have all the drugs we have today. We didn’t have the knowledge about how effectively we can rescue patients with myeloma. Many patients are opting for delaying transplant today. Just published in the *New England Journal of Medicine* was one of the largest studies comparing the outcomes of patients who had delayed transplant versus patients who had upfront transplant. In the context of up-front transplant, that first remission lasted 2 years more in patients who got transplanted up front versus the patients who opted for delayed transplant. Interestingly, at this time—with 7 years of follow-ups—the survivals are the same

I always tell patients, “Transplant is a choice. It’s not a necessity. You need water. You need love. You need air. You need food.”

Transplant is a choice you make based on conversations with your physician, based on the perception of how you’re going to do with or without a transplant. What do I think is significant? If you have not had what we call a minimal residual disease (MRD)—negative complete remission to your primary therapy, you should

seriously consider getting high-dose melphalan. Those cells that are there are the cells that are resistant to the best drugs that we have available. High-dose melphalan has been shown to effectively get rid of those resistant cells and put you into an MRD-negative complete remission.

In an older patient with low-risk disease who achieves a complete remission to primary therapy, you can think about maybe I want to delay it. Although, again, the DETERMINATION study showed that first remission is going to last a lot longer if you have a transplant up front. We do think that, unfortunately, salvage transplants and second transplants are underutilized in the United States. Only one out of three patients who relapsed on the TERMINATION study actually got a salvage transplant, as opposed to seven out of ten in the French study.

Now Dr. Richardson has said, well, that's because the survival is the same, but it's not just about survival. It's about how many lines of treatments, how is the response of the patients who did not get transplanted versus those that got transplanted as salvage. The DETERMINATION study teaches us a lot. The field has changed a lot in 10 years, so we now do quadruplets, but I do think that high-dose melphalan is here to stay for at least a while.

Mary DeRome (MMRF): If Rich had chosen to get an allogeneic transplant from a donor, how hard is it to find a bone marrow match?

Sergio Giralt, MD: That technology has also changed. When Rich was going through this conversation, we talked about it. I also recommended that we do an autologous transplant. Although he had extensive bone disease, he had no high-risk features. At that time, you had to have a ten-out-of-ten match. With the advent of technology that we call posttransplant cyclophosphamide, we can do mismatched transplants with results that are comparable to fully matched transplants. In 2022, everybody has a donor.

Mary DeRome (MMRF): Emily, for patients who have completed induction therapy and then they had a stem cell transplant—or even if they didn't get a transplant—what happens next? What is measured and what is the goal of the response? How do you want to see patients respond to that initial line of therapy, which may include a transplant?

Emily Patterson, NP: Whether it was induction therapy without transplant or after transplant, restaging would occur, and that includes blood monitoring. Some of the levels that Dr. Giralt was mentioning, the free light chains, you can remeasure the beta-2 microglobulin. There's a myeloma panel that should be checked, bone marrow biopsy to assess for MRD—looking for one in a million cells that is left behind after induction or transplant. Then repeat imaging if the patient did have myeloma outside the bone marrow detected on prior imaging before the transplant or before induction.

Restaging is usually done after this last cycle of induction or usually 3 months after the transplant is performed. This allows the body time to recover from the transplant and the chemotherapy that they received. Then, usually after we have the restaging results, we discuss maintenance therapy, which is often suggested to prolong and deepen a patient's response to either induction or transplant.

Ideally, we would have no MRD detected. The bloodwork that we checked would have no evidence of myeloma, and imaging would have no evidence of myeloma. Regardless of whether or not a patient had all these results showing no myeloma versus MRD, we would recommend maintenance therapy.

If there is active myeloma, meaning more than MRD, a further discussion is needed regarding whether or not another induction therapy line or further treatment, after transplant more so than maintenance therapy, is required.

Mary DeRome (MMRF): Regarding MRD testing: is it at the point where it's a standard process at most doctor's offices? When is the best time to get MRD tested?

Sergio Giralt, MD: There is a commercially available MRD test, which is monitored by Sequentia. It is a bone marrow test. You have to get a bone marrow aspirate to do it. It gets sent to a central lab, where it gets done. The other ones that we do, particularly in large academic myeloma centers, is flow cytometry. Both of them can measure between one in a million to one in 100,000 myeloma cells. Obviously, the lower the number of myeloma cells that are detected, the better. Many of us believe that it should be standard. It is not standard yet, though Sequentia is available across the country.

When should it be done? We think that it should be done in patients who've achieved a complete remission or a very good partial remission. That's where it becomes informative.

We know that patients who have MRD negativity at the 1-year mark posttransplant are patients who are unlikely to relapse within the first 2 years after that test. Patients who have an MRD positivity at the 1-year post transplant, 30% of them may have to deal with their disease within the next 2 years. It does differentiate.

What we don't know yet—and studies are being planned—is if I have a patient who's MRD positive, should I try to convert them to MRD negative by adding something else? Will that change the natural course of their disease? Those are studies that are being done, what we call MRD-guided treatment. Dr. Luciano Costa did a very interesting study, MASTER, in which patients who had sustained MRD negativity for 2 years were allowed to come off lenalidomide maintenance.

Those patients do not seem to be relapsing if they were standard risk. If they were high risk, those patients are relapsing. We're learning that some people can come off lenalidomide and not relapse. But the STAMINA study also showed that, if you stopped lenalidomide, your risk for relapse was almost twofold higher over the next 3 years than if you stayed on lenalidomide maintenance.

Mary DeRome (MMRF): Rich, what was your response to your initial therapy? Did you have MRD testing?

Richard Knox: I found out earlier this afternoon that I did. Dr. Giralt would report to me, but he never called the MRD testing to my attention.

As far as my treatment is concerned, I am on Revlimid—and for a long time: I was 28 days straight. Then I shifted, maybe 3 or 4 years ago, to 21 on, 7 off.

My wife thinks of the Revlimid-lenalidomide treatment as Pac-Man, just going along, eating up the myeloma. We made the decision a couple of years ago to continue on that therapy. I've been very fortunate. One, it was nice to have Welchol in my life. I had no significant side effects at all. Now whenever I'm off Revlimid for any duration of time, we get sort of freaky. Last month I had hernia surgery, so I had to go off Revlimid, because I was taking aspirin, for 2 weeks, and that just seemed too long.

As Emily was saying, it's important that the patient and the caregiver feel active in taking care of themselves. That's part of making sure that I'm faithful to the Revlimid, all the other pills I have to take, and stuff like that.

Mary DeRome (MMRF): We're up against the clock here. Dr. Giralt, can you quickly tell us about maintenance therapy, what it is, and what drug is most commonly used?

Sergio Giralt, MD: Maintenance therapy...this is again where clinical trials are so important. To everybody on the webinar, if you are offered a clinical trial, seriously consider participating. It is what establishes the standard of care today and will establish the standard of care tomorrow.

In 2010, we did what's called the CLGB 10104, which was a similar trial that the French were doing, randomizing patients to maintenance therapy with lenalidomide versus placebo. At that time, there was a lot of doubt that continued treatment would actually make a difference in myeloma.

There were people who said, "Oh, you're just going to make the cells resistant. Why don't you just leave them alone, and then when the disease comes back, you put them back on lenalidomide?" Lo and behold, not only did the remission from the transplant last 24 months longer, but people actually lived longer. This

study was done through the Bone Marrow and Transplant Clinical Trials Network and the CALGB, the Alliance. If you think of the number of years this intervention has saved, we're talking about hundreds of years of lives saved by this clinical trial, and it's now the standard of care. The French had said, "We only do lenalidomide for 2 years." The STAMINA trial suggests that no, you should continue until progression.

Lenalidomide is the most commonly prescribed maintenance. It's prescribed anywhere between 5 and 15 milligrams. Now it's common to give that week period that that Rich was talking about. In patients with high-risk disease, we're learning that lenalidomide alone may not be enough. There are clinical trials with bortezomib and lenalidomide, which show favorable results.

Clinical trials with lenalidomide and daratumumab are currently under way, which also suggests that for patients with high-risk disease, there may be a benefit for the combination. Dr. Francesca Gay just reported the FORTE trial, where lenalidomide was combined with carfilzomib. That maintenance strategy was better than lenalidomide alone across all patient categories.

I do think that we are going to see combined maintenance therapy as continued treatment for patients. The goal is to give people the longest life with the best quality of life with the right amount of treatment.

Mary DeRome (MMRF): What advice would you give a myeloma patient who's navigating treatment options and the question of transplant or not?

Sergio Giralt, MD: The thing I always tell patients, inform yourself. Go to websites like the Multiple Myeloma Research Foundation. I strongly encourage them to talk to a patient who's going through the journey. You also strongly encourage them, if you're a physician, if your local oncologist is not a myeloma expert, to get a second opinion with a myeloma expert. It is worthwhile. You don't have to change treatment. You can stay with your local oncologist, but it's worthwhile.

I'm a transplanter. I strongly encourage patients to get transplanted, because that first remission, that longer remission that's shown in DETERMINATION makes a serious difference.

Mary DeRome (MMRF): Emily, what are your parting thoughts to patients about transplant?

Emily Patterson, NP: Something that I learned from working with Dr. Giralt for many years is that with all these studies and the data that we have, we're looking at a forest and each person is a tree. Treatment is not one size fits all. There are many reasons to consider one induction therapy versus another, transplant versus non-transplant. You want to be comfortable that the provider that you're

with is looking at you as an individual and using the data at large as well. They're looking at the comorbidities that you have, how your disease presents, your response to initial therapy, your age, your performance status. Meaning how strong and robust you are.

Be comfortable that your provider is looking at the whole picture. I work in transplant, as well. Transplant is, generally speaking, the best way to prolong and deepen your response to initial therapy. But you need to be a good candidate for that, and you also need to be in a good mental space to prepare for that. Not everyone is, and that's okay. It is a choice. The best thing is proceeding based on all these factors and that also your provider is treating you as an individual.

Mary DeRome (MMRF): Do you have any parting thoughts, Rich?

Richard Knox: When I was diagnosed, unfortunately, the church I was serving at the time had other ministers die of cancer.

So how do you do it? I decided I was going to be up front all the time. When I was in the hospital initially, Nan would give reports on where I was doing. I got back and I used the analogy of the red convertible. You buy a red convertible, and then the only cars on the road are other red convertibles. That's exactly what happened to me once I had multiple myeloma. I appreciate the wisdom Emily has shared about talking to other people about it, and I'm happy to do that. I've enjoyed that. It's been important to me, and I hope it's important for other folks.

In a very real sense, it's a change of lifestyle that the patient and the primary caregiver has to go through. But I appreciate the ongoing care that Dr. Giralt and the team, including Emily, has given me for now a decade. I'm also glad to share and talk with other people, though everybody's cancer is their own.

As a social ethicist, I'm really willing to tell a lot of people how to live, but I'm not willing to tell anybody how to handle their cancer.