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Nancy Lajoie – a multiple Myeloma survivor

Operator: Thank you for standing by. My name is Krista, and I will be your conference operator today. At this time, I would like to welcome everyone to the Multiple Myeloma Updates Conference Call.

All lines have been placed on mute to prevent any background noise. After the speaker's remarks, there will be a question-and-answer session. If you would like to ask a question during that time, simply press star followed by the number one on your telephone keypad. And if you would like to withdraw that question, again press star one. Thank you.

I would now like to turn the conference over to Jennifer Gillette. Jennifer, you may begin.

Jennifer Gillette: Thank you, Krista. Yes, my name is Jennifer Gillette, and I am the Staff Social Worker at the National Bone Marrow Transplant LINK. I would like to welcome everyone to our Lunch & Learn with the LINK today. This program will focus on Multiple Myeloma Updates. A special thanks to our generous sponsors, the Leukemia & Lymphoma Society, Johnson & Johnson, and Incyte. We also thank our esteemed LINK partners.

Just so everyone knows how our program will go today, you will have a couple minutes of introduction about the National Bone Marrow Transplant LINK, and then we will hear from our health professional, Dr. Hamza Hassan. And then, we will hear from our survivor speaker Nancy Lajoie, and then we will open the floor for questions for approximately half the call.

For those who may not be familiar with the LINK, our mission is dedicated to helping individuals and their families from diagnosis through survivorship. We provide resources, support, and education.

Some of the resources we provide to help families navigate their transplant journey are our Lunch & Learn programs like you are on today that are on a variety of topics,

whether survivorship or disease specific information like what you are listening to today. We have our podcast, our Marrow Masters program. We have had almost 30,000 downloads to date with these programs and they are on again, all types of topics related to Bone Marrow Transplant or Graft Versus Host Disease (GVHD). We have webinars in the fall and those are usually on survivorship or Graph Versus Host Disease.

We have our Coffee Klatch program where people get a chance to talk with others who have gone through a similar journey. We have our peer support program. And our celebrate 2nd birthday because when you have a Bone Marrow Transplant, you get to celebrate two birthdays the year, and our Survivors Guide Book Club, as well as other programs. So, if you stay posted with us on Facebook or if you look at our webpage @ nbmtlink.org, you can connect with all these great services, as well as we have some books that I know are in high demand, especially with our LINK sponsors and partners. So, reach out if you need more support.

A couple of housekeeping items, we do ask that you please try to be concise with questions so we can answer as many as possible. Your line will be muted after your initial question has been asked, but you are welcome to re-enter the line with additional questions. We also know that the information provided in this program is meant to stimulate conversation with you and your own healthcare provider and not meant to replace your individualized medical plan.

So, now, on to the educational part of our program, Dr. Hamza Hassan is the Assistant Professor of Oncology in the Department of Medicine, Myeloma and Amyloidosis Division of Roswell Park Comprehensive Cancer Center and the University at Buffalo in New York. He is the Co-Leader of the Clinical Disease Team of Roswell Park's Multiple Myeloma division. He believes the future is bright for patients with Myeloma and Amyloidosis, with encouraging research and treatment development opportunities. He moved from Boston to Buffalo to join the team at Roswell Park Comprehensive Cancer Center to continue his work. Although both conditions are largely incurable, he shares that they are very treatable. So, there is a lot of hope. There is a great deal of translational research and clinical research that he is involved with that he believes will have the potential to help the field immensely and make a difference in patient's lives. Thank you for being with us, Doctor.

Hamza Hassan: Thank you so much for that kind introduction. And hello to everybody dialing in for this phone call. I really appreciate the kind introduction. I only see Multiple Myeloma and Amyloidosis patients and focus on these mainly and related illnesses. The topic that was given to me to talk about today was the newest treatments and updates along with some information related to bone marrow transplant and discussed some novel therapies including cellular therapies and T-cell engagers in full disclosure. This is very diverse, and this is the thing that excites us because we have so many good options and this is such an important topic that I discuss with patients every day.

I will start with a few of the little background things and kind of sketch. A usual course of how a Myeloma patient undergoes treatment during the disease course.

Dr. Philip McCarthy says, before the new drugs came out, treating Myeloma was like waiting for a taxi, and none would come. And then, all of a sudden five would come at once. During the time I have been treating Myeloma, we have like 17 new drugs over last 20 years. So, that comes out to be about one new drug coming up every year and I want to emphasize, this thing that I and Dr. Nikhil Munshi, (who I used to work with), felt like there is hope after hope at each stage for many of our patients. If not yet, there's continued research that I have collaborated with investigators nationwide, investing a lot of time in the laboratory, discovering new targets. So, I think this analogy of waiting for a taxi is still true and we are just going to keep getting better to trying to find a cure for this illness. There are about 36,000 new Multiple Myeloma patients diagnosed each year. Usual treatment costs will include patients will undergo induction therapies that will include three or four medications, which will include either monoclonal antibody targeted against our target known as CD38. There are two of them out there, Darzalex and Sarclisa, along with a proteasome inhibitor, which is injection or an IV or something that is given in the skin in combination with the pill, which is an immunomodulatory drug. Many of you would have heard the name Revlimid or Lenalidomide and Pomalidomide, and then lastly the Dexamethasone.

This disease does undergo four to six cycles of induction, and then if they have been transplant eligible and the treating provider thinks that they can undergo transplant, they are offered to do so. When I see a new patient, I kind of think what I am going to do for them first line, what I am going to do second line and third line, to be honest. I think that over the last two years, this has continued to change every time, with more and more data is published and then we learn more effectiveness of some of the newer medications and look for products that I'll talk about at the end.

So, for the time being, this really means the Standard of Care is for patients to undergo induction therapy (plus or minus a bone marrow transplant). If they are eligible for transplant, do the transplant. Then they either get a few cycles of consolidation, which can be omitted if they have a great response and they are on maintenance therapy. This has a hand in keeping the myeloma away for as long as possible. The whole goal is to control the myeloma numbers and the abnormal proteins, to keep them in a sleeping stage for as long as possible while maintaining the patient's quality of life. So, that is the most important two things that go hand in hand. No drug is a good drug if the patients cannot tolerate it, irrespective of how effective they might be. So, I think that is why this is not a cookie-cutter approach. All patients are kind of treated individually because each patient is different with their patient characteristics, how many commodities they have with their disease characteristics, whether they have the kind of myeloma that has high risk features, low risk features, and then the treatment for some already existing conditions that kind of limits our ability to use some of the commonly used medications that I mentioned so far.

So that is what we do, and then our hope is that the myeloma remains away for as long as possible. The response to this remission kind of depends on each patient. There is this box that we use of characteristics that kind of tells what kind of characteristic the myeloma abnormal plasma cells have, and they define what a high-risk disease is. I think it's a moving field when we talk about high risk because many patients in the past, we used to say chromosome 13 abnormalities is highest and now we don't talk about it anymore just because we have learned that our newer medications are able to

abrogate some of or nullify some of the effects. So, there are certain characteristics that now we think are high risk and what it means is these are the patients who are possibly more likely to have the myeloma come back sooner than later. Meaning, the remission might not be if in someone who does not have those features. When the relapse happens, it could happen in the form of a newborn lesion or in the form of blood count getting worse, or in the form of the myeloma blood number changing. It is then discussed how to start and how to treat. I think it is very it is very relevant to think of what they are, what their myeloma has been exposed to in the past and now there is this newer ideology, one I firmly believe, and what they are refractory to not just only what they are exposed. For example, if someone cancer is progressing on one of the immunomodulatory drugs while being on that drug, it is likely that their myeloma at this time is resistant to that particular drug and the response to that is that drug is used in this immediate second line might be suboptimal. We might lose this drug in the future, if we run out of options with combination of different drugs because there is this ideology that one plus one could be more than just two and one. I tend to use the more commonly used newer drugs that someone has never been exposed to. So, I hope to draw a good picture amongst some of the things related to bone marrow transplant. It is really not a transplant as such that you don't get another person's bone marrow. You get your own stem cells back, and it is more like a stem cell rescue. The way this works is there is a medication known as Melphalan that we have been using for the last 50 years, the first time in 1958. The high dose Melphalan came into being in 1983. So, this has been out there for quite some time and that is all what we had for quite some time. We learned it kills the myeloma cells very effectively, but it also kills the good cells, the stem cells, and other cells. So, the process of stem cell transplant includes harvesting your stem cells. We give them shots that kind of make those stem cells that live in the bone marrow come out and circulate in the blood. We put a catheter as I mentioned and then we collect those stem cells from the blood. We just store it just like a blood bag and then we give this high dose Melphalan that kills all good and bad and hopefully get rid of whatever the minimal amount of myeloma might be remaining after the induction. After that, we give those cells with the same patient back to them as a stem cell rescue. There is no chance to minimal chance of any graph versus host disease, meaning this is not a foreign bone marrow that is getting infused back into the patients. We then wait for the blood counts to get better. When they get better, the signs that the bone marrow cells that the stem cells that we give back to the patient have found their home back in the bone marrow, we call that time when their blood counts look good as engraftment.

When I was at Boston, we worked at a program where we used to do outpatient transplants. So many patients can go home daily, and they will have to come in once a day. We even get that for our patients at Roswell Park Comprehensive Cancer Center. We have both models. We do it on a case-by-case patient basis, but when able, staying out of the hospital also means lesser chances of infections and each patient makes their own decision along with their transplant team. Patients do get assigned to transplant coordinators as it is a team effort. I think it is always important to emphasize the use of clinical trials and many of the drugs and the combination of the medications we are using now used to be clinical trials. I always encourage patients if I have a clinical trial option available, because that tells the next Standard of Care and most of the clinical

trials are in the best interest and they are testing either the medication that has already been proved to be great or they are offering a new horizon or new hope to test some of the newer medications.

With that, I will switch to some of the novel treatments. While we are talking about relapse, the drugs that have not been used, we try to use them as second relapse as the first relapse or like a second line or third relapse or a third line and some of the new already exciting treatments have been these cellular therapies and T-Cell Engagers. We were included in Phase 1, the very first clinical trials of these patients. And we collect T-Cells which are some of the cells that kill anything foreign in our body if it gets in. Myeloma has found a way to camouflage itself. So, we collected T-Cells from their own T-Cells, from the patients, engineer them in a way that they can identify the myeloma cells in the lab and then we give those T-Cells back to the patients. They find the myeloma and they try to kill them. There are side effects that come with it. The newer side effects that we are still learning, but that is the gist of CAR-T therapy.

The different targets that we can use are where there is new hope. There are two more commonly FDA approved ones. The one commonly USDA approved one targets BCMA or B cell maturation antigen, Carvykti or CAR T-cell therapy. There is also Abecma. Lastly, the T-cell engager is another kind of immunotherapy. It is a bispecific antibody and there are three that are FDA approved. Two of them are kind of par with the same target. The BCMA as I mentioned and the third one targets a different one which is a G-protein-coupled receptors. A handful of words but GPCR5D. We can do different sequencing to try to get control of myeloma. There are many newer medications on the horizon `, something which are newer generation of immunomodulatory drugs like the Lenalidomide or Revlimid and Pomalidomide or formulas that I mentioned earlier. Some are Iberdomide and Mezigdomide. These are some of the things that are coming up along with many other receptors like FcRH and these are drugs that we are just learning more and or how to combine two targets in the CAR-T, how to give something else that makes the CAR-T kind of last long, or make it affect longer. So, these are the things on the horizon and with that, I will hand it over to Ms. Gillette.

Jennifer Gillette: Thank you so much, Dr. Hassan. That is very inspiring and I am excited to see those things come about. And thanks for such a thorough presentation.

And yes, our next speaker is Nancy Lajoie, she is a woman dedicated to family and friends, and her adult child. She is in a new phase of life and is able to share the reality of treatment in a way that will make you giggle. She also has stories of beauty from those that have stood by her. She also leads a group called “Lift Us Up” at her church for cancer survivors. Prepare to be inspired by Nancy. Thank you for joining us.

Nancy Lajoie: Yes. Thank you, Jennifer, and Doctor, thank you. I love what you said about “waiting for the taxi.” I will have to remember that was a good definition of the new drugs on the market.

On my story, I was diagnosed at 47 with colon cancer, had a resection and an appendectomy. I did six months of chemo and then I made it to remission. Somehow, I knew I was going to live, I believed I had a purpose, but at that time I certainly did

not know what it was. And then in 2019, I hemorrhaged and had, I was told, my uterus was the size of the piece of paper, and I had a cancerous mass. So, I was sent immediately up to Rochester, and I had a hysterectomy and I beat the odds by 2%, which is truthfully incredible. In 2021, I was diagnosed with multiple myeloma, high risk, I should say, my free light chains were the kappas were 11.75 and the lambdas were 0.41. So the nephrologist, a kidney doctor, diagnosed me. I was immediately sent to the oncologist here in Ithaca, and I was, well I was stage two out of three, and I was told it is high risk meeting. I think there is about 13% of us that are high risk, meaning that I carry the lovely extra chromosome or one chromosome, I guess is malfunction. I asked approximately how long, and they said about 40 months or so. So, I went and had my port put in and I had a PET scan and I had a bone marrow biopsy and my teeth were all cleaned because I would be going on some medicine which is to strengthen my bones and it affects the teeth and so forth. I started treatment. I did Darzalex. I took Revlimid pills. I did Dexamethasone, which is a steroid. I also did Velcade, and they gave me two Benadryl's and a Tylenol before each treatment that was twice weekly. I have so much gratitude for my newly made friends. I only knew them maybe a year or so, and they all signed up to drive me to my treatments and stay with me. Some of the side effects that I had were unfortunately, neuropathy hives, cramps, and some lovely peeling skin on my stomach. It was kind of interesting because it looked like kind of a snakeskin. Apparently, it just happens to some people. So, I lather up with lots of lotion on those days. I gave up driving and shopping when I was on the steroids. Well, many of you probably have taken steroids before I took for seven weeks. I lived on 4 hours of sleep and at 4:00 am, I would hop on QVC and I ordered about $2,000 worth of Christmas presents for everyone. As crazy as that is, the boys got this and the

women got that. I was then referred to the Wilmot Cancer Center in Rochester at that time and she said no, no, Nancy, this is not a Sprint. It is a marathon. And we must manage your side effects of chemo. They wanted me to have as close to a normal life as possible. The doctors consulted and agreed to cut my meds in half, about halfway through treatment. And I think one of the things that is truly most important is I thought that I had to be that sick to kill the cancer cells. I have since learned to speak up and that is so important. Learning to speak up and tell your nurses, tell your doctors, your nurse practitioners, your P.A, how you are doing and how you are feeling. I did start documenting on my Facebook page and I thought truly, that "oh, people would just scroll by it because they're not that interested." I was so touched by the overwhelming response and so many people told me that they learned so much from my experience. I was shocked, really, truly shocked at how people had reached out to me. And sometimes when I am feeling down, I will often re-read the words of love and support which does truly help, and after a few months of intense chemo treatment. I was cleared for the stem cell transplant and referred to the bone marrow transplant team at Rochester. And they gave me a little book on stem cell transplant. Truthfully, I will be honest, I was very scared when I had read a couple of pages and then I would put it down. I would pick it up again, put it down. But my daughter helped me make the decision by emphasizing that I needed to choose an option. The option that would give me the best quality of life as long as I could, so the BMP was the option. Plus, I found that I would not have to actually drink the intense chemo. I thought that I had to drink that, but when talking with my doctors, they said, "No, no, no, Nancy, it's given via

your port intravenously." So, I was on board and I had to fill my cheeks with ice cubes chips for about 45 minutes before, I believe its called cryotherapy. That was to help with mouth sores and esophagus sores, which I have none, which was wonderful actually.

I had the stem cell in April of 2022. I was in the hospital for about three weeks or so, and I thought it was kind of funny that I felt like an egg in the incubator. But they were right, in about a week or so, all my blood counts bottomed out. I lost my hair in one day. I had to wear a lovely helmet that the orthopedic staff fitted to my head because when your temps drop, of course that means your platelets as well, which is your blood clotting. If I were to fall or something, there would be, obviously, damage if I did not have my helmet on. So, as soon as your blood counts right off, then you can take your helmet off, but my friend here sent me cute stickers to put on my helmet and I think I was the only one on the floor getting mail, which was a real boost actually, when you're kind of confined to your room and not being able to go out. I have two best friends that I truly cannot thank enough who traveled across the country to stay with me. Each one took a month when I finally got home and they were so careful and keeping me from not getting sick, they cleaned my house all the time, even so I wouldn't have any dust when I wanted to go out on the porch. I mean, they were just fabulous. The idea is that you do not… when you do go outside, like if someone's mowing or whatever, you do not want to breathe that air. You have no immunities, really to fight anything off. And I had no plants inside my house and none outside and so forth. You do not eat any raw food, and everything must be cooked. But truthfully, you do not really have that much of an appetite. For some strange reason, I loved mashed potatoes and cooked spinach, and I do not know why.

When I got a few months out, I got my childhood vaccinations all over again. And then I hit the year mark and I started to feel like me again. I had originally let my hair grow back in gray, and I was so excited I had curls. But they did not last. When I looked in the mirror somehow it did not look like me, so I dyed it back to my natural color and it just gave me more peace and joy. I think it is because you lose so much of yourself sometimes and you just want to see you again. My friends often will call me a warrior and I think you have to feel like one. I think these warriors just do not give up. They keep going.

One of the hardest parts is that no one knows what to say to a cancer patient. I remember showing up to Thanksgiving dinner with my family, with my curly hair and a mask, and everyone stared at me, and they did not know what to say. And I think it is up to the cancer patient sometimes to break the ice because you are still the same person on the inside, no matter what your cancer diagnosis is. You are still a mom and aunt, a sister, or a friend. And what helps me in the long haul is the stem cell transplant was definitely worth it. I remember my team, Dr. Al, as I will refer to him, and he says, "Oh, Nancy, you're going to do great." And my brain is thinking, "Oh, you probably say that to all your patients." But afterward, when I met with him, I told him about this and I said, doctor, I don't know how you know, but you just know that this is going to work and I'm pretty much that the two-year mark, and I feel like I said I do feel like

myself. I am kind of living the best life. I can go to plays, I can go to dinners, I can go to concerts. If there is I am cautious, I do have low immunities, and so forth. But I am so grateful to be here, and I have a will to live.

I still get DARZALEX once a month. They started B12 shots and I get those once a month. And I also get IVIG in my Gal-1 once a month also, just to keep in my Gal-1 gs up to around 1100 or so and that has helped a lot also.

I think I truly have found my purpose that I mentioned earlier. I think my purpose is to help others. And I started volunteering at Infusion and helping patients talk with them, hold their hands. They look at me and they see someone healthy, and they go, "You have cancer?" And I said' "Yes, I do." And I think to hope is to believe, and I think that the patients need to remember this, that to have like the doctor said, the taxi waiting for the taxi for new drugs on the horizon, new treatments, and so forth. I did start a church group called, "Lift us up" only because I was approached by two different people that had cancer, one of which was multiple myeloma, and I spoke with them for about an hour, and he was just so happy. He has not had a stem cell transplant yet, but he is going through chemo, and he said my words just helped and he knew kind of what to expect. And when I came home and my heart was just as big as my house, I swear. And I said, "This is it! This is my purpose." So, it just came to me, and I said, well, we will start this little group. We get together, and we talk, and we support each other, which is a wonderful thing. I think being grateful, and I know that probably sounds to share whatever, but being grateful every day and you can see the wonder just some simple things like I think having cancer changes you, it changes your perspective on things. I think, just being grateful for simple things like sun, or trees, or flowers, or whatever a child's smile, a grandchild. I think that is very important to be grateful. And like I said before, warriors do not give up, we keep fighting. And I think that also to give that back and to be kind and just try to give back in what I am doing with a little group and then volunteering at Infusion. And it took some of the focus, I think, off you and that there are other people just like you that are going through many of the same things. I think it really helps. So that is pretty much my story.

Jennifer, I do not know if you would like to step in.

Jennifer Gillette: I sure would. Thank you so much, Nancy. We really appreciate you sharing your story. And I am sure you are helping people today with that story. And Krista, could you please tell our callers how they can ask a question if they have one for either the doctor, Nancy, or both?

Operator: Certainly. If you would like to ask a question, please press star one on your telephone keypad.

Jennifer Gillette: Thank you. From our waiting clip, I am going to ask one question and then we will get to those calls. One person had written ahead of time. If kappa and lambda are high but the M spike is not, should you worry? What are your thoughts, Doctor?

Hamza Hassan: So, this is at the phase where this is being made. There are two things that matter. If one is more elevated than the other and the proportionality seems very odd, that obviously deserves further investigations with biopsies like bone marrow biopsy to see if there are any clonal or kind of identical plasma cells present in the bone marrow. The other piece is our body does produce a higher amount of kappa light chains, free light chains, I should say, than lambda free light chains. If someone with kidney disease, it is likely that they will have a buildup of kappa free light chain more than the lambda. And sometimes both are elevated, but then the kappa is more elevated than the lambda. If someone has those kind of kidney disease issues, and the more we are learning, I think there is this big study in Iceland that is going on that is learning population dynamics. And they have screened the whole population, almost 75-80 thousand people to like…to learn what the normal ranges are. The ranges that we are currently using are as touch, but do they change if someone is in their 40s as compared to their 80s? I think that is the thing, we will get an answer on from those. But the bottom line, there are some eight specific variations in the lab ranges. In some of the kidney disease, kappa will likely be a slightly bit more elevated than lambda. The ratio might be normal or slightly on the higher side.

And lastly, they do not have kidney disease. I think then it does become to the proportions if the difference is like too much between them, I think then it demands further work up with the treating physician.

Operator: Your first question comes from Steven Valdivia. Please go ahead.

Steven Valdivia: I have been diagnosed as newly diagnosed ultra-high risk and I am looking at CAR T-cells options and concerned at the same time with side effects of like REVLIMID. I am 75 years old and I know that REVLIMID has a secondary cancer possibility at elevated ages and high risk. Is there another alternative I should consider?

Hamza Hassan: Sorry, go ahead.

Jennifer Gillette: Oh, no. Go ahead, Doctor.

Hamza Hassan: If I understood the question right, seventy-five newly diagnosed myeloma. I probably did not understand for a newly diagnosed, I do not feel that currently, CAR T is kind of given upfront unless in a clinical trial. There is a trial ongoing and soon opening Cartitude-6, which is comparing CAR T upfront as compared to industrial plus transplants. There are risks elaborating on secondary malignancies and obviously, I did not go into some more specifics. The ultra-high-risk disease is obviously a thing that I focus on a lot, and it depends on how you define that. And there is progress that is being made and these are the patients who we really know the patients who we want

to focus on, and there are some dedicated studies that are being done for these patients. Like from the UK, that is this optimum study, which is the phase two study, there is a concept trial, but many of the treatment with myeloma. I think they do come with some side effects and some of that has affect the quality of life and some like which are already mentioned, with steroids and some of them do have further risk.

The REVLIMID has a potential risk of further leukemia and DES to develop. And the more we are learning is it is like cumulative exposure over years, there is risk of skin cancers as well. But patients when they do get it, they are very closely followed with a skin specialist for the CAR T. I think it is just so new for us to kind of really…it will definitively. There has been an update in the passive label that whenever I convince or kind of present the data on CAR T, I do tell patients that there is a risk of some kind of T-cell malignancy that were reported in patients who were treated with one of the CAR T products. And is it just a hint or…and then it is kind of also like is it because these

patients have been treated for so long for so many other things and all of them is this is an additive effect. Or is it really the thing that is coming out of CAR T it is just yet to be done? Nevertheless, that based on the year 2024 information, I think that we do disclose these things. Both do come with risk. The way I see it. And then at the end, I think we do end up to one decision based on the response rate, patient preference, what they are able to tolerate. How far do they live from the center, that is another thing like CAR T that cannot be done in a very small medical center. And both have some risks, but we have a handle what is at present, to do entertain some of the things that will come down the road. My hope and wish is that we did not have a treatment that has those effects that come down the road, but we are not there yet.

Steven Valdivia: Thank you.

Jennifer Gillette: Thank you so much. Can we have the next caller, please?

Operator: If you would like to ask a question, please press star one on your telephone keypad. Your next question comes from Nancy Escobedo. Please go ahead.

Nancy Escobedo: Hello. I have a question for the doctor. I had an autologous stem cell transplant almost a year ago. I am currently on my maintenance treatment with DARZALEX and Lenalidomide, and according to this protocol I am on, I would continue that for two years. So far, my labs have all been essentially normal. I am just wondering, after my two years is up, what is the next treatment course for me? Thank you.

Hamza Hassan: You know, this is a great question. And I kept my talk earlier with these because this is the thing that I wanted to give as much time. And as people have said, this is like a marathon, not a sprint. And I do want to talk something about supportive care towards the end and it integrates to your question. The short answer to this question now, for

how long do we continue the maintenance, which is kind of the hand on the part to keep it away is not known. That there is this study from Charlotte Powell, UK, where they did do a big study looking into for how long and this is for REVLIMID only. Whether four years is fine, whether three years is fine, we do know that there is this marker known as MRD, naming minimal residual disease or measurable residual disease that I will mention in a brief. Where is the status of that thing? How many side effects are there? Is it positive or negative from MRD? How much value effect is somebody having from DARZALEX and REVLIMID? And what is your age? The cumulative exposure, or how much of that am I thinking? I think for two years, for three years it does make sense to continue it. After that, we really do not know if there is added benefit or not. I think when there are these situations and there are no clear kind of guidance. One group of physicians have always thought that we kind of continual progression at least the REVLIMID. The studies that were being done and

there is a reason more paper that pursues trial, they did kind of deescalate, meaning got rid of the DARZALEX if someone was MRD negative after a certain number of times. But there is a group of those patients who did need to go back on it just because the MRD they became positive. And is MRD the thing based on which we should add or minus things? It is also an area unknown. I always encourage these in full disclosure. I think these are individual conversations and the best person to answer this is with someone who has all the information from cytogenetics risk or what is the MRD set as harmful side effects somebody is having, age for how long they will be able to tolerate it, and what are the quality of life effects that they have.

I think having a lot of…so that is what I would conclude that. But I do think the supportive care part that I was mentioning, I want to say when I see patients I kind of do focus on four main things. Their bone health, as I mentioned, the Zometa, the most friendly medicine is very important to prevent the fracture to happen. The steroids used, many patients have their sleep affected, cataracts develop, blood pressure get disease, diabetes develop. Those are the things that we as clinicians' kind of ask people to do know not to let go of not only treat the myeloma but treat the patient. The risk of infections, obviously the DARZALEX in this situation, as you were mentioning, we do know that it does come with a relatively higher risk of infection. But do they lead to serious infection that leads to someone admissions or critical enough that makes them to have an organ affected? I think they do not at the end of the day. And then I think it is also very important to focus on your kidney health because as we know, many of these myeloma abnormal proteins are not healthy to the kidney. We do recommend people to minimize the use of any painkillers unless they really do and Tylenol is their friend if need to be. Just to be prepared for this matter and to be in as good shape to get the best next treatment whenever the myeloma comes back.

Jennifer Gillette: Thank you. Thank you, doctor. Do we have more calls in the queue?

Operator: We do. Your next question comes from Donald Swart. Please go ahead.

Donald Swart: Yes. I have been in cancer treatment for myeloma for about two and a half years now. I started out with a high dose of forty milligrams of the steroid dexamethasone. I could not take it. I have what you call costochondritis. I believe that is what it is infection in my ribs and stuff like that. So now I have…for 2 1/2 years I am down to one steroid pill. A 4 milligram pill a month and I'm taking injections of DARZALEX. That is what they call it. And then I got VELCADE and now that is worked for me because my life changed, went from 80 down to six. Now, since probably about six months ago, it started going up a little bit. It has been going from six to eight to nine and now I am at 11 and now my doctor wants a PET scan taken of me. And I have been doing fine until just probably about two weeks ago in my treatments of

two injections, and then I have a VELCADE then I have my other two injections again. So, all in one month, one steroid pill a month. That is all I can take because that takes me…that keeps you away for a day and a half. I only get about 3 hours of sleep with that. But now it seems like my VELCADE kind of wears off in a week because I have been having some back issues, right and left the ribs, in my back. When I breathe, when I cough, it hurts, stuff like that there. I just woke up right now that I had it all the way till yesterday. Today I woke up, I had very little back pain, but it's been a week since my VELCADE has been injected in me. So now I woke up this morning with seven hours sleep, no bathroom trips. Usually it is two or three, and I guess I am wondering why. Why does this suddenly change in one day? It must be the VELCADE. Am I correct? Because my doctors prescribed that PET scan for me soon because I have also had a swollen leg which they had a…they were afraid of a blood clot. And it is just my left leg and my left ankle. My ultrasound came out good, so I do not have a blood clot. Do you have some information that I can absorb here?

Hamza Hassan: So, I am going to summarize two of the questions. If I got those right. One is like what could be the back pain from, and then the second is about the use of steroids when the 4 milligram is okay along with DARZALEX and VELCADE. For the back pain I think the most relevant thing, whenever we think about these somebody who is myeloma is in control and your back pain is happening, I would do exactly the same as your physician is doing to look at the PET scan and actually looking at the low dose CP portion of the PET scan to make sure there is no non-avid meaning, not lighting up kind of disease on the CT scan. A development of a newborn lesion is one of the possibilities in that area, or a previous lesion could be present lesion, meaning the spot on the spine. If you had one, if you had in the beginning, one of the previous spots can get worse, then that can be responsible for the pain even if the myeloma is in control. Because the way I think is like these bone lesions, there could be…many a time they are not that calcified even with giving Zometa and vitamin D and whatnot and activity is everyone's friend. I think that the previous lesions can get worse even with controlled

disease and then new lesions can develop that do justify if through with change in therapies or control at the local site.

About steroids, I think using as much as is doing the job is the right answer and there are two uses of that. One is to have the MP myeloma effect, meaning controlling the myeloma. Another is decreasing the risk of infusion or injection reactions from the DARZALEX. If it is working for those two with four, I think…and it is making you feel okay and function because that's the most important thing in this picture. I think 1 + 1 + 3, there is some additive effect the does would not be three always but then and it might be low, higher. And when a small amount of the dexamethasone might still be doing its job if the other ability of you be able to function is still intact.

Jennifer Gillette: Thank you. Do we have any more callers?

Operator: We do not currently.

Jennifer Gillette: I have one more question and this one is for the doctor. One person's rights given the wildly published statement, most of all, multiple myeloma will relapse. A question of quarterly blood checks is sufficient and if no symptoms means no worries, what are your thoughts about that case?

Hamza Hassan: I think that quarterly monthly blood work with symptom checks is probably the way we got to let people have and live life to the fullest during the time of the myeloma [indiscernible] and the time at the earliest time of the symptoms to develop, meaning the bone pains or worsening function that can sometimes be like just worsening fatigue. Something that is not going away for a week or so, despite doing everything and you do your blood pressure check, and you develop a fracture. That is not normal. Those are the things you must bring to your myeloma doctors' attention. And if the lab numbers are looking okay, I do think that we do not instill much more worry. But then remaining connected is the key because we do know, as rightly said, the myeloma does come back.

I do think that remission is something which can be defined in many ways, and there is like…and that is the gist of the answer. The remission can be defined in many ways. And is it MRD meaning one in a million cancer cells by 10 raised by -6 of a threshold negative, if someone's PET scan is also negative? I think the combination of those two are really reassuring and there is this analogy of tip of the iceberg, which is always used. You know, the blood work can only tell you the circulating blood cells recirculating a normal protein. With bone marrow is something that might become abnormal much more sooner. Now I am not a fan of having…not any patient to go through the bone marrow as it is so invasive, it is uncomfortable. But in selected patients it is the thought that should we be doing bone marrows earlier and then once a year or even farther out. I think post-test we can do one after one year. And then we

do on…we do use the blood as a reflection of what is going on in the4 bone marrow. Because at the end of the day, the diseases of the plasma cells present in the bone marrow and the most accurate detection is by analyzing the marrow itself.

Jennifer Gillette: Thank you so much. I appreciate that.

Hamza Hassan: This has been great. I think that one thing that was mentioned about the quality of life as a result of post-transplant, I think that is one thing which is so good that there is an immediate effect that this quality of life is affected. But we do know that the progression-free survival, the PFS with many of your physicians would talk about was noted to be longer along with some benefits and quality of life. You shout out to a lot of these transplant coordinators who were behind the scenes but are in front of the scene, the nurses, the support staff, IPPS and everyone around. And of course, the fellow collegial myeloma, BMP, and CAR T colleagues, and the patients and the caregivers foremost, who inspired us all every day.

Jennifer Gillette: Well said, doctor. That is beautiful. And I love what Nancy said too about that you do not have to be as thick as possible to do well as well as piggybacking with what you just said. It is quality of life in addition to quantity. But I thank you both for an amazing presentation today. I thank everyone for being here. Our sponsors, our LINK partners. As well as I want to let everyone know, I know there was a lot of information today and there is going to be a recording on our website within a few days as well as a transcript from today. We will also be sending out a survey. If you could take a moment to fill that out, that would help us to provide the best programming possible for you. But on that note, I hope today helped you in some way, and thank you for being a part of us.

Nancy Lajoie: Thank you, Jennifer, and thank you, Doctor. I learned some new things.

Hamza Hassan: Thank you. (inaudible)

Operator: This concludes today's conference call. Thank you for your participation and you may now disconnect.