Hello everyone. On behalf of The Leukemia & Lymphoma Society (LLS), a warm welcome to all of you. Special thanks to Dr. Melissa Alsina for volunteering her time and expertise with us today. We have over 2,000 people participating in today’s program from across the United States as well as other countries, including Canada, Colombia, Indonesia, Ireland, Poland, and Tanzania.

We would like to acknowledge and thank Bristol Myers Squibb, Genentech & Biogen, GlaxoSmithKline, and Takeda Oncology for support of today’s program.
Following the presentation, we will take questions from the audience. We are also audiotaping and transcribing this program for future posting on our website.

March is Myeloma Awareness Month. The Leukemia & Lymphoma Society is a champion for myeloma patients, caregivers, survivors, and families. Multiple myeloma is among The Leukemia & Lymphoma Society's primary research initiatives. LLS currently has over 30 active projects, which is an over $40 million commitment in multiple myeloma, focused on laboratory and clinical research.

Together with our volunteers, patients, researchers, healthcare professionals and supporters, we are determined to change the future from myeloma treatment and care. Our vision centers on driving new breakthroughs and cures, helping all myeloma patients access the care they need to survive and thrive and addressing healthcare disparities that disproportionately impact underserved populations.

PRESENTATION

Lizette Figueroa-Rivera, MA

I am now pleased to introduce Dr. Melissa Alsina, Senior Member of Blood and Marrow Transplant and Cellular Immunotherapy program, and head of the Multiple Myeloma BMT-CI program at Moffitt Cancer Center in Tampa, Florida. Dr. Alsina, I'm now privileged to turn the program over to you.

Melissa Alsina, MD

Thank you, Lizette, and welcome everyone. I want to thank The Leukemia & Lymphoma Society for the invitation to participate in this event and also for everything they do to help our myeloma patients.
So, today I will talk to you about treatment updates in myeloma. These are my disclosures.

And I will start by giving you a brief introduction. I think if you're in this call, obviously, you've heard about myeloma; but some of our patients have been just recently diagnosed, so I will go over a brief introduction about the disease before going into the ways that we have to treat the disease.

So, what is multiple myeloma? Multiple myeloma is a cancer of plasma cells. And in this screen, you see those cells are like oval with light lilac cytoplasm. Those are the plasma cells. And the plasma cells, we all have them. They live in our bone marrow which is inside of the bone where all the cells of the blood are formed. And these plasma cells are part of the immune system, and they're functionally produced antibodies which is a type of protein to help deal with infections.
So, these plasma cells can grow like any other cell in our body, I guess. And when they grow, and they're more than 10% of all the cells in the bone marrow, that is diagnostic of myeloma. Because the normal function of these cells is to produce these antibodies, these proteins, when they grow, they keep producing that. But they only produce one type of antibody, and they produce these antibodies in very high amounts.

And the reason why this is important is because measuring these antibodies or immunoglobulins, another way we call this is the M spike, like the monoclonal protein, it's the best way to follow the disease. It's the best marker of the disease and that gives information about how the patient is responding to therapy or when the disease is getting more active.

Myeloma is a rare disease accounting for only 1.8% of all new cancers in the United States. However, it's the second most common cancer of the blood after lymphoma; and in the United States there were 32,270 patients diagnosed with myeloma last year. And there are about 140,000 patients living with myeloma or in remission.

It affects more adult patients. Median age at diagnosis is 69. But we don't see everything. I'm a myeloma specialist, so I only see myeloma patients. So, my youngest patient is 27, and I've seen, obviously, patients in their 80s as well.
So, what happens when you get myeloma? Well, these cells start growing in the bone marrow, which is where the cells of the blood are formed. So, patients frequently can have low blood counts, especially red cells which are the cells that carry the oxygen. So, patients with myeloma can present with tiredness, weakness because the cells that are affected are part of the immune system. Your immune system can get weakened by the disease, and patients can have frequent infections. Patients can also have kidneys being affected. We see that in about 30% of the patients. And that is multifactorial, but it could be from the proteins being created by the cancer cells affecting the kidneys and also by the fact that the calcium in the blood can be high as a result of damage of the bones; and that can also affect the kidneys. And finally, a patient with myeloma can have bone damage. If you're a patient with myeloma, you are probably presented to a doctor. The most common presentation is the patient that presents with bone pain, persistent bone pain. And when they evaluated that, they found that there were some myeloma cells there affecting the bone, and that's very common for myeloma.

A small percent of myeloma patients present with no symptoms, and when they have no symptoms, and the markers in the blood or in the bone marrow are not very high, I would say though that those patients have smoldering myeloma, which is a more indolent form of the disease. And some of those patients don't need therapy, just observation.
So, how do we treat myeloma? So, I think the treatment of myeloma has evolved a lot, you know, over the past 20 years and continues to do so. I would say every year when we go to the hematology meetings or to a myeloma meeting, more studies are presented with new drugs; and it's changing the way we treat. So, because of that, it's very important that if you're a patient with myeloma, you seek the advice of a myeloma specialist because even though it's a rare disease, it has a very complicated treatment paradigm; and we have many treatment options.

But in general, I would say that when you start therapy in myeloma today, in 2021, the goal is to achieve a complete remission. Complete remission is, if I do a bone marrow biopsy, I will not see any myeloma cells and I will see no areas of cancer in your body. This is not the same as cure, right, because the patient can be in remission, but the resistance comes back later. And that is what happens with myeloma. But if the patient, we're able to get the patient in a complete remission, then that response is more likely to last for many years as opposed to a patient that we cannot get in remission.

In the past, we didn't even bother to get a patient in remission because we did not have the tools or the good drugs to be able to do that. But things have definitely changed. And now we give initially, when we have a newly diagnosed patient, we give induction, which is usually a combination of three or four drugs. Now we are into four drugs, followed by consolidation with a bone marrow transplant using the patient's own cells; and this is for patients that are transplant eligible.

We've learned over the years that maintenance therapy is very important, so we've continued maintenance. And then eventually when the disease relapses and comes back, fortunately, I mean that's obviously not good news, but the good news is that we have many treatment options for those patients as well. And I will discuss some of those today.
So, talking about the newly diagnosed patients, I will discuss with you some of the new data. So, this study that I'm showing here is called the GRIFFIN study, and it was a study done to look at what would happen if you add an immunotherapy drug which is a monoclonal antibody that is called Darzalex® or daratumumab (dara). You might have heard of these.

And patients were newly diagnosed that were considered transplant eligible, were randomized to receive the standard of care which would be something like Revlimid® (lenalidomide), Velcade® (bortezomib), and dexamethasone (dex) versus the same treatment but with the addition of daratumumab which again is a monoclonal antibody against the protein expressing the cancer cells.

And then patients would get four cycles of that which is about three months of therapy, followed by a transplant; and then after that they would receive more treatment with dara and D-RVd (daratumumab, lenalidomide, bortezomib and dexamethasone) versus RVd (lenalidomide, bortezomib and dexamethasone) and then the maintenance, also daratumumab-Revlimid versus Revlimid. So, the lower path, the one that isn't that great, it is more or less what is standard of care and this study challenging that and saying, "Well, if I add this immunotherapy drug, maybe we'll do better, right, and we can get more patients in complete remission."
And the answer to that is that, that actually helps. And it was showing that if you keep treating the patients, the responses get better if you keep giving this treatment, right? So, if you look at the first bar at the end of induction, we only have 19% of the patients in complete remission. But by the end of transplant and consolidation, you have actually 80% of the patients in complete remission. So pretty impressive.

And this group here on the left, which is the group that got the Darzalex plus Revlimid, Velcade, and dexamethasone D-RVd and the group on the right where you see that at the end of treatment the complete remission rate was 60.8% as opposed to 80% complete remissions.
The other thing that was very good with this study is that we looked at minimal residual disease (MRD). So minimal residual disease means that the patient is in remission, right? I cannot see any cancer cells. However, there could be some cancer cells that are left, and I cannot see them. Right, my level of detection with the normal studies that we have cannot see that.

So, there's new tests now that we can do to see if there's anything left when a patient is in remission, and some of these studies can detect one cancer cell in a million cells. And getting to this meaning of the zero-disease negativity is important because this correlates with better signs that it's under control and better survival.

So, this is, even though right now we're still learning whether we do need to get every patient to that minimal residual disease may not be studied, we do know that patients that get there are going to do better. And in this study, I think I see on the left, in the purple area, patients with MRD-negative that got the dara, Revlimid and dex were 51% versus 20%. So, this is probably one of the reasons that the four drugs, patients that receive four drugs did better with these combinations. And this is true, what I showed you before was after transplant, but this is true also after maintenance which is 62% versus 32%.
And then there is another study that was just presented at the hematology meeting back in December where patients got Kyprolis® (carfilzomib), which is a drug like Velcade. It’s a different proteasome inhibitor, with either Revlimid or Cytoxan (cyclophosphamide), they got four cycles; and then they were randomized to receive a transplant and further consolidation therapy versus no transplant, so continue therapy with Kyprolis-Revlimid and dexamethasone. And this is one of the stories that is trying to answer that question, do I need a transplant? You know, nowadays we have so many drugs, do I still need to do a transplant? At the end, patients were randomized to receive Revlimid maintenance only, which is standard, versus Revlimid in combination with Kyprolis.

And these are here the response rates. As you can see, the groups that got the transplant, which are the ones at the left where you see KTd (carfilzomib, thalidomide and dexamethasone) ASCT. That ASCT (autologous stem cell transplant) means transplant, and KRd (carfilzomib, lenalidomine,
dexamethasone) transplant versus just continue therapy on the right. As you can see, response rates are good, right? But in terms of MRD-negativity and also complete remission, which is the yellow bars, those are better when you do a transplant.

And then if you look at the time that the patients, the time, the disease stays under control, also during the transplant, which is the blue curve showing 78% is better than not doing the transplant, which is the green curve. So, this is one of multiple studies that have shown over the years, but this one is very recent that transplant is important.

So, to summarize these results, if a newly diagnosed patient gets Kyprolis-Revlimid-dex and transplant, they have prolonged time with the disease under control. This was observed through all groups of patients, patients with standard risk or patients with more aggressive myeloma, high risk.
And also getting maintenance with the combination of the Kyprolis and the Revlimid versus the Revlimid by itself was better in terms of how many patients got to that deep response state of minimal residual disease negativity and also time with their disease under control.

And this is just to show you, I told you before that if the patient gets to that MRD-negativity state, those patients do better; and this appears to show this. This is a different study that was done years ago, but it was also a patient getting just transplant, I mean Revlimid-Velcade-dex followed by transplant versus no transplant. And as you can see in the curve, if you look at the top two curves, the red curves on the top, these were patients that were MRD-negative and definitely did better than patients that were MRD-positive. But also, if you get a transplant and you're MRD-negative, you still do better than if you did not get the transplant and are MRD-negative.

So, we're still learning what to do. I think when we test for MRD in a patient and we see that the patient is MRD-negative, we get excited. Right, we say, okay, this patient is going to do better and so on. But we don't have data yet to say, okay, I can stop medications. Right, I can go ahead and stop, for example, the maintenance. We don't know that.
But we do know that patients that are minimal residual disease-positive would do better if they would become negative, so we are doing studies now trying to adjust our treatment to get to that MRD-negative state to get better outcomes.

And so, in general, these are different trials for patients that are newly diagnosed and can be transplant eligible. And as you can see, I wanted just to share these, a busy table, but I just wanted to show you how better we're doing in terms of complete remission rates. Right, in the past, we would get 10% of the patients in remission which was really disappointing. But nowadays we're talking up to even 95% of the patients getting remission, and many of these patients getting MRD-negativity.
And again, this is for newly diagnosed patients, transplant eligible.

And this is another curve showing how MRD is important predicting survival, and we just already talked about that, so I'm going to skip this for the sake of time.
So, what about even for patient that is not a transplant candidate, and what makes a patient a transplant candidate or not? Well, it's not really age, chronological age, but more histological age. Right, you could be a 75-year-old patient and be active, healthy, no cardiac disease, no other comorbidities, and you could be a transplant candidate as opposed to a 55-year-old with heart disease and diabetes and obesity that we wouldn't be able to do a transplant. So, the decision about transplant versus no transplant is something that you need to discuss with your doctor, and then depending on your specific situation, you know, you decide.

But even though I showed you in the slide before that doing a transplant was better than not doing a transplant, patients that cannot do a transplant have also very good treatment options. And this is the latest recommendations from the NCCN (National Comprehensive Cancer Network), which is like a cancer network where a lot of specialists get together and give recommendations about what the best treatment is. But I just want to show you that in the preferred regimens, even for patients that are not more frail patients, right, three drugs are recommended in three out of the four categories here. So, we know that combining these three drugs is better than just two for frail patients.
And I wanted to present you this data because the most recent one is very good; and this study again, like that GRIFFIN study that I shared at the beginning, uses this daratumumab-based antibody against the protein expressed by the myeloma cells in combination with Revlimid and dexamethasone and compared that to just Revlimid and dexamethasone. So, no antibody, and this is for transplant-ineligible patients.

And again, we saw that the addition of the antibody in red here, right, you see the overall response rate, 92% versus when you don’t give the antibody, 81%. But the most compelling thing is the fact that you get a much higher number of patients in CR (complete response), right, almost 50% when you add the antibody versus about 24% when you don’t add the antibody.
So, remembering that the goal of therapy is to get the patient in complete remission because that translates into better time, longer time the disease is under control, and better survival. And this is, the time frame is progression-free survival, which means the time that the disease stays under control, right, before relapse. And as you can see, it was better for the DRd, the Darzalex, the Revlimid, and the dexamethasone versus the Revlimid alone. And also getting to that MRD-negative. I mean if you look at the second graph, the lower graph, you can see patients that got DRd, dara, Revlimid, dex and MRD-negative, their progression-free survival is pretty impressive, right? That curve is actually up there and not going down.

And these treatments are well-tolerated. I mean with Revlimid you get sarcopenia. With Darzalex you can get some infusion reactions. Even though Darzalex was recently approved to be given as an
injection under the skin, it works the same, it has the same efficacy, but it actually has less side effects. So that is the way to go with Darzalex.

So, I would say that if I see a patient that has newly diagnosed myeloma and is not a transplant candidate, my treatment of choice would be Darzalex-Revlimid and dexamethasone. However, a patient could also get Revlimid-Velcade and dexamethasone and get a good chance of getting complete remission like I circled in this table. So, I would say Revlimid-Velcade-dex at an adjusted regimen, so it's better tolerated, versus dara-Revlimid-dex, either one is a good option.

Okay, so I talked to you about what that initial treatment entails. So, to summarize, if you're a newly diagnosed myeloma patient, you should get three drugs up front for induction or four with the addition of the Darzalex followed by transplant, followed by maintenance therapy. And if you're not a
transplant candidate, then you should get three drugs at least with very close follow-up to that response. And treatment could be adjusted, you know, if we're not getting where we want to go; and, again, the goal should be to obtain a complete remission and, if possible, minimal residual disease negativity.

Now unfortunately, even when we do all this and we get very good responses and we get a high number of patients in remission, the history of myeloma is that eventually that disease will come back and will relapse. And that is, obviously, the bad news; but the good news is that we have many good treatment options also for that patient population.

And I am not going to talk to you about all of them but only the new ones, which, actually, there are a lot of them that are new. So, we're going to go over several treatments; but, again, these are not the only options.

So, I'll talk to you briefly about a drug that is called Xpovio®. The other name for it is selinexor in case any of you have, it's a new class of drug, and it has a very different mechanism of action. This graph here, what it shows, the kind of purple part is like the nucleus of the cell; and the other, the base part is the cytoplasm. And there's a pump in that nuclear membrane that takes things out of the nucleus of the cytoplasm and vice versa. And this pump sometimes is taking out proteins that can make the cell die, the cancer cell dies. So, this drug, Xpovio or selinexor blocks this pump and allows for those proteins that can induce cell death and death of the cancer cell to stay there longer in the nucleus. So, it's the only drug in that class.
And it's an oral drug, and it's approved for patients in combination with dexamethasone, for patients that have failed more than four prior lines of therapy. It's taken by mouth. And in initial studies, it was given twice a week, but more recently studies have shown that it can be taken once a week. And recently it was approved to be given in combination with Velcade and dexamethasone for patients that have failed only one prior therapy, so quite early in the course of the disease.

So, if you give the drug with just dexamethasone by itself, the response rate is 26%. But this was in patients that were very heavily refractory. So, patients that have received all the other standard of care therapies and the disease would still get active.
Now this study combined Xpovio-Velcade and dexamethasone, right, and it was also randomized to Velcade and dexamethasone only versus that combination. And as you can see when you start combining these drugs, then the response rate goes significantly higher; and then we're talking 76% in the group that got the exposure with Velcade-dex versus 62%. The reason why this 62% is different than what I showed you before, 30%, is because in the prior studies were patients heavily pretreated, refractory to all different kinds of therapies. And in this study, patients had only failed one-to-three prior therapies, so it's early in the course of the disease; and usually when you give drugs earlier in the course of the disease, they work better.

The main side effect of Xpovio or selinexor is nausea and vomiting. That is the worst. It's an oral drug, gastrointestinal symptoms. And the best way to deal with that is to be proactive. So, you want to take medication for the nausea before you start the drug. So, the night before and then the day that you
take the drug and the day after take medication for nausea, even if you don't feel nauseated. So, the best way to deal with this is with prevention, and usually if you do that, the patients do quite well. So, it's something to discuss with your doctor if you're going to get this drug. And the patients can have fatigue, low blood counts, low sodium in the blood, but again, the most significant ones are the gastrointestinal effects; but importantly, these can be prevented.

So, enough of selinexor. We're switching to another drug that is called melflufen. And for those of you who have received a transplant in the past, you might remember that before you got the stem cells, you got chemotherapy that was called melphalan. So melflufen is the same as melphalan but in a fancy package, fancy delivery package. And this drug, studies have been done. It's shown to be effective, and it was submitted to the FDA; and the good news is the study was approved like just a few days ago. It was approved actually last Friday. So now we have yet another option to treat our patients.
And this is the study that led to the approval of this drug. This drug is given in the vein every 21 days along with dexamethasone. It's only one dose on day 1, and then you repeat in four weeks. And then you take dexamethasone the other weeks. So, dexamethasone weekly, three weeks on, one week off, and then melflufen, one. And this is a response of all the patients. The response rate was about 30%, and this is only with dexamethasone.

And most common side effects of these drugs, like from melphalan, is actually dropping the count. And interestingly, in patients that were what we call triple-class refractory, so these are patients that the disease is still active, even when they have received Velcade or Kyprolis or Darzalex or Revlimid, and we see that in this patient population, it still works and also in patients with extramedullary disease. That means that the disease is growing outside of the bone marrow. This is a patient that could have a tumor of plasma cells under the skin or in the lung or in other areas in your body or in the lymph nodes.

So good drug and effective and just approved, so one more option that we can use.
Then we have this one, iberdomide. It's a different drug. This is in the same class as the Revlimid and the Pomalyist® (pomalidomide), and this study was done in patients with relapsed myeloma and also a good response rate, upwards of 30%. And at ASH (American Society of Hematology), the hematology meeting just in December, they presented data of this drug in combination with Velcade and with Darzalex and with response rates like about 50%. So again, when you combine these drugs with other drugs, they work better.

Okay, we're going now to the cell therapy. I would like to talk to you a little bit about this BCMA that you might have heard. So, this means B-cell maturation antigen, and this is a protein that is preferentially expressed like a myeloma cell. So, it's a protein that is expressed by the myeloma cells and contributes to the myeloma cell growth. But you don't see it in other cells. So, because of that, it's a good target. It's something that you could target because it's only in the myeloma cells.
So, the first group, they're called antibody drug conjugates. And these are antibodies. It's like a protein, like is shown here in the figure, that can only go and bind to that BCMA in the myeloma cell, but it carries a toxin with it. So, when the myeloma cell gets, the antibody gets on the cell, the cell gets that antibody inside of the cell, and then the antibody releases that toxin and causes cell death.

And we have one ADC (antibody drug conjugate), right, approved in myeloma that is called Blenrep or belantamab mafodotin. Very complicated name but we can just try to remember Blenrep. And this is given in the vein also every three weeks, and it was approved for patients with relapsed myeloma that have failed more than four prior lines of therapy.
And this was the overall response as you see in the table on the left, about 30%. And the main issue with this drug is that it can cause corneal problems, so it can cause ophthalmic toxicity or toxicity to the eyes.

So, patients need to have an ophthalmologic evaluation before they start the medication and before each dose. So, it's a little bit controversial, but the drug can work. It's a new novel mechanism of action, so it's something to consider if the patient has relapsed myeloma and have failed four therapies, this would be a good option.
And then going to CAR (chimeric antigen receptor) T-cell therapy, which is probably the treatment that has all of us the most excited these days because of the efficacy. Right, I'm going to try to explain how this works; but essentially these are new cells from the patient, so lymphocytes that we collect from the blood. These are not stem cells like we use for the transplant. These cells are taken to the lab, engineered so that they can recognize that BCMA protein that we talked about before.

So, this is sort of a cartoon that will help me explain a little bit more how it goes. So, this is what CAR T stands for, chimeric antigen receptor T cell, and this is what's going on in your body. Right, you have your myeloma cells. The myeloma cells have this green marker which is BCMA. And then you have the immune cells. So, you have a few immune cells and a lot of myeloma, and the immune cells are not specific enough against the cancer, and they're not big enough. Right, they're not big in number. They're not numerous enough to attack the cancer.
However, you can take these cells, the immune cells and you can actually make them CAR T cells, which means that you get a DNA set of the cells that make them express an antibody against BCMA. And then you not only do that, but you grow these cells. So, now you don't have just a few cells with no specificity against the cancer, but you have a high number of cells with specificity against the myeloma, against the BCMA.

And then this is what happens. You give the cells back to the patient, and those cells go and attack the myeloma and kill the myeloma cells and actually overwhelm the myeloma. So, this is how CAR T works.
In more practical terms, I'm going to spend a little bit of time talking about these products, bb2121. Ide-cel will be the commercial name because this is the one that is going to approve probably in about a month from today. No more than a month from today. So, in more practical terms for the patient, and this is the way the study's done, if you look at that, then there's like an arrow, like a green arrow. So, patients come for a screening, which means you come, and we do tests, we do check your heart, your lungs, the myeloma, do a bone marrow biopsy. Somewhat similar workup to what we do pretransplant. Then we do leukapheresis, which means that we collect the cells from the blood. Those cells are sent to be manufactured, and that manufacturing takes about four to six weeks. So usually in the meantime while you're waiting for your cells to be ready, we give the patient treatment to try to keep the myeloma from getting more active. And then the patients get chemotherapy for three days through their Revlimid and Cytoxan. This is done outpatient, and then two days of rest, and the day before they admit, the cell infusion, patients are admitted to the hospital; and then the cells are infused. And the cells are given in the capillary. They're given in the blood. And then we follow. Patients usually have to stay in the hospital for two weeks, at least for this study. We keep the patients in the hospital for two weeks, and then another two weeks close to the center where you got the CAR T cells. So, patients usually have to be close to the center where they got the CAR T cells for four weeks.

And this is the initial study that was done with this product that is going to be approved. And, as you can see, patients were heavily pretreated, about six prior lines of therapy. Ninety-two percent of the patients have received already a transplant before they got this, and close to 100% of the patients have already been refractory to Revlimid or Pomalyst or Velcade or Kyprolis.

And these are the side effects. You know, your patients can have low counts. That is the most common. And then patients can have something that is called cytokine release syndrome, CRS. And that usually happens very shortly, like a day or two after you get the cells. And it's like your immune system is so hyperactive that patients can get a fever, low blood pressure. But we know how to treat this complication, so even though these patients would get that and could get that for a few days, in the majority of the patients, that was able to be resolved. We saw that in actually 75% of the patients,
but in the majority of the patients it was a mild form. We only saw a more significant form in 6.5% of the patients.

And then the overall response, which is, you know, it's pretty dramatic, it's actually 89.5% and about 40% of the patients actually achieved remission; and many of these patients achieved minimal residual disease negativity.

The downside or the, I guess, disappointing thing is that the duration of response is only about 10.3 months if you count all the patients. If you count only the responders, it's about 12 months or a year. But when we treated the patients in this study, this was given to patients that had absolutely no other option very late in the course of their disease, so we know that if we treat patients early on when a patient has failed, for example, three prior therapies as opposed to eight, the duration of response is likely to be better. And there's studies ongoing already using these products early on in the course of the disease for patients that have more high-risk form of myeloma.
And I'm going to skip this for the sake of time.
And then the other problem that is coming, but we don't know yet when it's going to be approved, is the same type of problem, CAR T against BCMA, and it is a Janssen product, and they did the initial study. They have already treated 97 patients in a Phase I and a Phase II study.

And the responses are very impressive. As you can see, 96.9% overall response rate and 67% complete remission. And in this study, they didn't have enough follow-up to tell us for how long that responses last. But it looks like very, very effective product as well.
The patient population is very similar to that earlier one.

So, 27 out of 29% of patients at six months have still not progressed.

So, it seems that this is going to be a good product. We don't know yet when this is going to be approved, and toxicity is very similar to what we saw with the other CAR T.
So, this is just a table to show how it goes. If you're going to get CAR T, you have to go to a CAR T center, sort of like a transplant center. And then you get the cells collected, the cells go to the manufacturer. It takes four to six weeks. Then once they're ready, then you come get the chemotherapy for three days, two days of rest, get the cells, and then you have to stay in the center for four weeks. And two of those weeks, in the clinical trials, those two weeks have to be in the hospital; but I suspect that once it gets approved, probably patients will be in the hospital for one week and then the other three weeks outpatient.

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<td>Not reported</td>
</tr>
<tr>
<td>CRS, all grades (G3/4), %</td>
<td>62.5 (0)</td>
<td>79 (0)</td>
<td>70 (41)</td>
<td>17 (0)</td>
<td>45 (0)</td>
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<tr>
<td>Neurotoxicity, all grades (G3/4), %</td>
<td>4 (4)</td>
<td>16 (5)</td>
<td>22 (7)</td>
<td>4 (4)</td>
<td>0</td>
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<tr>
<td>Duration of response (mos)</td>
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<td>Not reported</td>
<td>17</td>
<td>Not reported</td>
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</tr>
<tr>
<td>Median progression-free survival (mos)</td>
<td>18.8</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
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</table>

*No graft-versus-host disease; 1 Two deaths

So, these are not the other. These two that I mentioned to you are the ones that are closer to be approved but are not the only ones. But there are other CAR T cells, and even CAR T cells when we, if you see in this table it says, "ALLO-715." That means getting CAR T cells from another patient, not
from the same patient. So, all these studies are ongoing. They all have promising results, and it will be probably other things coming up in this sense to improve our results in the next few years.

Then the other treatment that is also targeting BCMA immunotherapy, these are what we call BiTEs, which stands for bispecific antibodies and T-cell engagers; and it means that you actually have a protein, an antibody that not only binds the BMCA in the myeloma cells, but it has another part that can bind an immune cell. So, it brings the immune cells in close proximity to the myeloma cell, allowing for the immune cell to kill the myeloma cells. So, it's like making your immune system closer to the myeloma cell so that it can kill, it can do its job killing the myeloma cell.

And these are some of these drugs. None of these are about to be approved. They're still in clinical trials. But if you look at the overall response, you know, we see 62%, 69% overall response. So,
these are active drugs. And this is easier, right, to give. Some of these are used sub-Q. You don't have to collect any cells. So, this is easier than doing a CAR T. But still early on. So, I think in terms of these BCMA-targeted therapies, the CAR T, the bb2121 is the first one that is going to be approved probably in a month. And this will follow in the next few years.

And these are others that are also in clinical trials; and again, so far, we're seeing good response rates, 69%, 53%.
supportive care before this therapy to prevent the nausea and vomiting and be like proactive about that.

I talked to you about Blenrep which is also approved to treat patients that have failed four prior lines of therapy. It works very well in combination with dexamethasone, and I think it's going to work better in combination with other drugs. And those studies are ongoing right now, but I'm pretty sure that by the end of the year, we'll get more information on those.

We have iberdomide which is still in clinical trials, but we have actually melflufen that was just approved last Friday, another option. Then we have these treatments that are CAR T cells or T-cell engaging antibodies, which, as I show you, especially with the CAR T cells, they are very effective, they have manageable toxicities, and we're super excited to have one of these approved in a month. And I think having this treatment available for myeloma patients will clearly impact the outcome of these patients. And yes, these are very intense treatments; and they do have toxicities, but we have learned that these toxicities can be managed and, you know, these treatments can be tolerated.

So, I think with this I'm going to stop, and I will be happy to take your questions.

**Lizette Figueroa-Rivera, MA**

Thank you so much, Dr. Alsina, for volunteering your time with us today and to update us on the treatments for myeloma. I think this was one of the first times that we were able to hear that a CAR T-cell therapy is about to be approved, so that's very exciting to our listeners.

**QUESTION-AND-ANSWER SESSION**

**Lizette Figueroa-Rivera, MA**

It is now time for the Question-and-Answer portion of our program.
We'll take the first question from our Web audience. Doctor, Maria asks, "How does one continue to stay smoldering and not progress? Is there any treatment to keep it at that smoldering state?"

**Melissa Alsina, MD**

Yes, wow, that's an excellent question. So, patients with smoldering myeloma, they have a 50% chance that the disease is going to progress in five years after diagnosis. And if it hasn't progressed in the first five years, then the risk of progression gets lower. It becomes about 2% per year as opposed to 10% per year for the first five years.

Now there are patients that have what we call high-risk smoldering myeloma, and those patients will progress earlier. You know, instead of 50% chance in the first five years, 50% chance in the first two years. And for those patients, we have clinical trials that are being done. Some of them have been done here in Europe like using just lenalidomide and dexamethasone, and that has been shown to delay the progression of the disease. And then there are other studies that are very aggressive. You know, we are offering the patients like the best four drugs that we have to treat myeloma early on for patients that have high-risk smoldering actually with an intent to cure.

I would say, to try to answer your question, it depends on what type of myeloma you have. If you have high-risk smoldering myeloma, then my suggestion would be to try to find a clinical trial that can help. And if you don't have high-risk smoldering myeloma, then I would just do observation. I wouldn't treat you. And high-risk smoldering myeloma is defined as having two out of three of the following: more than 20% plasma cells in the bone marrow, an M spike in the blood of more than two and a kappa/lambda ratio or lambda/kappa ratio of more than 20. So, if the patient has two of the three, then that would be high risk, so you can discuss that with your doctor and see exactly where you are.

**Lizette Figueroa-Rivera, MA**

Thank you. And we'll take the next question from the telephone audience, please.

**Operator**

Our next call is from Linda from Massachusetts. Linda, please state your question. Your line is now live.

**Linda from Massachusetts**

Okay, thank you. Is the CAR T-cell as invasive or difficult for people that are not eligible for stem cell therapies?
Melissa Alsina, MD

No, no. No, because what makes the transplant in the stem cell more difficult or maybe some patients are not eligible is because with the transplant with a stem cell, we're giving high doses of chemotherapy. And that high-dose chemotherapy is very toxic and can be toxic to your heart, your lungs, your liver. So, if you're a patient that you're frail, you have other comorbidities, you might not be able to tolerate that high-dose chemotherapy. But with the CAR T, we are not giving high-dose chemotherapy. We are giving chemotherapy, but it's sort of a low dose just to suppress your immune system somewhat so that the CAR T cells that you get can go in your body and do their job. So, yeah, a patient that is not eligible for a transplant could be eligible for CAR T.

Lizette Figueroa-Rivera, MA

Thank you. And our next question is from Eddie, and it's what you were just mentioning. Eddie is asking, "What's the best way to determine if I am a transplant candidate?"

Melissa Alsina, MD

So, the best way would be to go see a transplant doctor, right, that specializes in myeloma. But in general, again, it's not based on age. It's based on more physiological age and general condition and how active the patient is and does the patient have any other organs that are affected, like someone with heart disease or lung disease, for example. And then the other thing that we consider in transplant eligibility is also where the myeloma is. If we have a patient that has received a lot of therapy and the disease has relapsed multiple times, those patients do not benefit from transplant. So, the best time to do the transplant is early on after diagnosis. You know, you get your initial therapy, get the disease under control and then do a transplant. If not, transplant doesn't work well when you leave it for the last minute.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from the telephone audience, please.

Operator

Our next call is from Jeff from Indiana. Jeff, please state your question. Your line is now live.

Jeff from Indiana

Hi. I was wondering, I was in remission for a while after taking Revlimid, dexamethasone and Velcade, and this time I'm taking in place of the Velcade it's Ninlaro® (ixazomib). And I was just curious if you could comment on Ninlaro as I've never heard of it before.
**Melissa Alsina, MD**

So, I guess Ninlaro is a drug like Velcade, the same class of drug, what we call a proteasome inhibitor, but it's an oral. It's given as a pill once a week, three weeks on, one week off. It can cause neuropathy also like Velcade but not as much as Velcade. And it's an effective drug in myeloma. It depends on what it's combined with. But it can be given in combination with Revlimid and dexamethasone. The approval of Ninlaro is in combination with Revlimid and dexamethasone.

**Lizette Figueroa-Rivera, MA**

Thank you. And along the lines of what you were just saying, Robert is asking, "Is there anything available to help my neuropathy?"

**Melissa Alsina, MD**

So, that's a big problem in myeloma. I mean the myeloma per se can cause neuropathy but also some of the drugs that we give like the Velcade, which I mean it's the biggest one there. So, it depends on what you're experiencing. If you're experiencing just numbness and not pain, the only thing that would help with that is time and waiting for that to get better. If you are experiencing pain, pain from neuropathy, there are several drugs that can be used for pain for neuropathy. One is called Neurontin (gabapentin), the other one is called Lyrica (pregabalin) and the other one is called Cymbalta (duloxetine). And these drugs, usually you don't do all of them together. You just do one or the other and then you try to optimize the dose. And in a neuropathy when it's painful, frequently patients feel it more at night, so sometimes we, you know, during the day because these drugs can make you sleepy and drowsy, you can take less of a dose during the day and then a higher dose at night.

There are other things that can be done like acupuncture. Some patients say that it helps, so I'd recommend a patient of mine to try that. The other thing that sometimes helps is a marijuana product, so seeing a doctor that can prescribe medical marijuana for neuropathy pain also could be helpful. And then some topical things. There are some topical creams like cocoa butter. There's a cream that is used for diabetic neuropathy for patients that have neuropathy from diabetes, and it's called Neuragen. Also, that could help. But I would say the main thing with a neuropathy is prevention, like if you're taking a medication like Velcade, for example, to make sure you pay close, close, close attention and the minute that you start feeling, like, numbness or tingling, you need to tell your doctor and that dose of Velcade should be adjusted or stopped. Because once it's established, it's a lot harder to deal with it.

**Lizette Figueroa-Rivera, MA**

Thank you. The next question can we have a telephone question.
Our next call is from Rania from Florida. Rania, please state your question. Your line is now live.

**Rania from Florida**

Hey, good afternoon, Dr. Alsina. One of my questions is after you've been on a therapy like Revlimid and Velcade, can you go back on the same therapy if the one you are on right now doesn't work?

**Melissa Alsina, MD**

Hi, nice to hear you.

**Rania from Florida**

Me too, Dr. Alsina.

**Melissa Alsina, MD**

You can. You can as long as the disease has not become active while you're getting the medication or within 60 days of stopping the medication. So, for example, let's say someone gets Revlimid-Velcade and dexamethasone at diagnosis, a transplant, then Revlimid maintenance and the disease, I don't know, several years later the disease gets active again, then you can go back to the Velcade, for example. And the other thing is that sometimes you can go back to a different combination. So maybe you're getting Revlimid-Velcade and dexamethasone and that's not quite working. Then maybe you can do Kyprolis-Revlimid and dexamethasone. You do a different one, a different combination and those could work. Yeah. So, normally we wouldn't go back on the whole, you know, like if you're on Kyprolis-Revlimid and dexamethasone and your disease is progressing on that combination, then we know that doesn't work so we will not try that again, but we would try other combinations.

**Lizette Figueroa-Rivera, MA**

Thank you. And Wynn is asking, "What do you recommend when one has an allergic reaction to Revlimid?"

**Melissa Alsina, MD**

So, that could be an issue sometimes. And my suggestion with those patients is that you talk to your doctor about doing desensitization. We think, you know, like when you were allergic in the past, right, when penicillin patients were allergic to penicillin and penicillin was such an important antibiotic, that
they would do desensitization. We can do desensitization to the immunomodulatory drugs like Revlimid-Pomalyst. And I would suggest to all myeloma patients that if you have that problem, you consider doing that because these drugs are such an integral part of the myeloma treatment, they're so important that if you're not able to take any of these immunomodulatory drugs, that could affect, obviously, the management of your disease. So, I would do that, and I think doing that in any patient that has an allergy to Pomalyst or Revlimid.

**Lizette Figueroa-Rivera, MA**

Thank you. And also, Batina is asking, "Are there any drug therapies for myeloma, single or combined, current or in the pipeline, that do not include the use of steroids as a standard of care?"

**Melissa Alsina, MD**

So, steroids are very important in myeloma because they kill the cancer cells, so they're part of the treatment. However, we can adjust the steroids. Like, initially when steroids were used in myeloma, patients used to take 40 milligrams daily, four days on, four days off. It was crazy. And we learned that we don't need to do that. We learned that we can get away with giving the patients only 40 milligrams weekly. But then we also learned that sometimes we don't need that much. We can reduce it and go 20 and even go lower. And sometimes we don't need the steroids. Like, if you have a patient that you give them the treatment, patient responded very well, you keep the patient on maintenance. You don't necessarily need the steroids at that point. So, I think you need to talk to your doctor if you're having trouble with the steroids and then try to adjust the steroids to a level that you can tolerate. But we usually try to give them if the patient can tolerate them because they're important to help control the disease.

**Lizette Figueroa-Rivera, MA**

Thank you. And we'll take the next question from the telephone audience, please.

**Operator**

Our next call is from Larry from Illinois. Larry, please state your question. Your line is now live.

**Larry from Illinois**

Yes. I had a stem cell in 2016. And after that, they put me on 10 milligrams of Revlimid for 21 days and seven days off. I have been on that ever since, and one of my doctors, as I go to Arizona for the winter, wants me to get off the Revlimid and the other doctor in Illinois doesn't say anything about that. And I just feel like the Revlimid is keeping me alive, so should I continue to take it or not?
Melissa Alsina, MD

Well, I mean something to discuss with both of your doctors in more detail, but what I would say is that the recommendation is that patients stay on maintenance therapy indefinitely. You know, there are studies that are ongoing that perhaps would answer that question more clearly, but the data that we have right now suggests that continuing that maintenance therapy is important. Now you may not necessarily to stay on that 10 milligrams. If you're having toxicity, they can drop it to 5. But if a patient of mine is not having toxicity, not having side effects on the treatment, then I would continue the Revlimid again indefinitely.

Lizette Figueroa-Rivera, MA

Thank you. And the next question is from Beth. Beth is asking, "What can I do to keep kidneys healthy during treatment in the course of my multiple myeloma?"

Melissa Alsina, MD

So, the kidneys, as we talked before, can be affected by the myeloma in about 30% of the cases, so we are usually very careful with the myeloma treatment with the kidneys in myeloma patients. So main thing is to try to stay hydrated, drink a lot of water; avoid any new medications that you don't know whether they could affect your kidneys. Discuss with your doctor early, "Is this okay for my kidneys?" And the other thing is avoid an iodine-based contrast. For example, if you need to have a CAT (computerized axial tomography) scan, we don't do iodine-based contrast because those can affect the kidneys. But the main thing, I mean the most important thing of all those things is try to stay hydrated, drinking a lot of water.

Lizette Figueroa-Rivera, MA

Thank you. And along that line, there are many folks asking about nutrition. Should they have a specific diet if they're taking medications for myeloma?

Melissa Alsina, MD

My answer to that is no. My answer to that is that you should have a regular diet, you know, healthy diet. But no. There's no strong data one way or the other, and I think like the same way we all should have a healthy diet to keep our organs – our kidneys, our heart, our lungs – healthy, become diabetic, it's the same. Whether you have myeloma or not, it's the same. So, there's nothing special about having myeloma and the nutrition. Obviously, there are stages in the disease. If you just had a transplant, for example, then, yeah, then there's a special diet you have to follow. But otherwise, no.
Thank you. And Paul is asking, "Is Revlimid-Velcade-Darzalex and Decadron (dexamethasone) the gold standard for myeloma free light-chain disease?"

Melissa Alsina, MD

My answer to that question is going to be yes. But that combination that you just mentioned is not yet approved by the FDA, so sometimes we have trouble. When we try to give Velcade-Revlimid-dexamethasone and Darzalex altogether for a new diagnosis, the insurance can say, "No, that's not approved." But yes. But I think if you follow that GRIFFIN study that I presented, definitely better responses, better minimal residual disease. So yes. I think while today it's not considered necessarily standard of care because it's not FDA approved; I think that it's not going to be too long. I mean I think probably this year that combination will be approved.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from the telephone audience, please.

Operator

Our next call is from MaryJo from California. MaryJo, please state your question. Your line is now live.

MaryJo from California

Yes. I wanted to know if you're on Pomalyst, can you have the COVID (coronavirus disease) vaccination?

Melissa Alsina, MD

Yes. So that is a very good question, MaryJo. Thank you. Yeah. The recommendation is that every patient, every cancer patient and myeloma patient take the COVID vaccine. We know that the vaccine is not going to hurt the patients. What we don't know is how the patients are going to respond to the vaccine. In other words, how strong of an antibody response your body is going to make to make actually the vaccine work. And we are actually in our center studying that testing for COVID antibodies after the vaccine and up to two years in the patients, the myeloma patients that are getting the COVID vaccine. But, yes, you should get it because some immunity is better than no immunity.

If you look at the International Myeloma Foundation, they have some general recommendations about like if you're on steroids, hold the steroids for a week before and a week after you get the vaccine. But there's no data to support that. So, if a patient can do that, that's fine but otherwise, we're giving the vaccine to everyone.
Lizette Figueroa-Rivera, MA

Thank you. And alongside your question, Caroline is also asking, "How do myeloma patients do when or if they contract COVID-19?"

Melissa Alsina, MD

So, unfortunately, myeloma patients do worse than the regular population and there have been a few studies published, both from New York, showing that if a patient has myeloma and gets COVID, the mortality rate is almost 30%, so it's pretty high. So that's also why it's so important that patients with myeloma get the vaccine and also keep following precautions like the social distancing, the handwashing, using masks because definitely in myeloma patients the problem is that what's causing the disease are cells that are supposed to be part of your immune system and they should be protecting you, right. And now these cells are causing myeloma and doing what they're not supposed to be doing. And the immune system in myeloma patients is definitely depressed, and the treatment that we use doesn't make that any better. So, yes, it would be at a higher risk than the general population to get COVID.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from the telephone audience, please.

Operator

Our next call is from Carl from Florida. Carl, please state your question. Your line is now live.

Carl from Florida

I'm having significant problems with my eyes, retinal degeneration. I was wondering if Revlimid may in any way be affecting my eyes?

Melissa Alsina, MD

Revlimid is not known to affect the eyes. I don't know if you're taking any other medications that could do that. The steroids can affect the eyes. And then as we talked, this new medication Blenrep, but that, obviously you would know. And then the other medication that can affect the eyes is Velcade, but it can cause like in the conjunctiva, like in the white part, redness; it can cause inflammation of your eyelids; infections in the eyelids like sties. And that's the Velcade but not the Revlimid.
Thank you. And we do have another question from Virginia. She's asking about Revlimid. She has chronic diarrhea from Revlimid, so she's asking, "Is there any other maintenance protocol available" or is there anything that she can do for the diarrhea?

**Melissa Alsina, MD**

So, yeah, that is a relatively common side effect to Revlimid, especially in patients that are on it for a long time like we do for maintenance. So normally what I do I try Imodium. It's over the counter and you can try that. If that doesn't help, there's another medication that is called cholestyramine or Questran®. And you can talk to your doctor about trying that. That helps several patients. But many patients none of that helps, and we just have to do a dose adjustment. And the important thing about dose adjustments for diarrhea is like, for example, if you're on 10 milligrams of Revlimid and you just drop it to 5, it usually doesn't work. So, you have to stop the drug, give your GI system, your intestines, a break to recover for about a month and sometimes longer and then resume the drug at the lower dose. So, you have to stop it altogether and then rechallenge with a lower dose if the symptoms go away.

And then you have to see. Some patients, for example, tell me, "Well I'm on the Revlimid. I do well for the first two weeks and then on the third week I just start having a lot of diarrhea." Well, if that's the case, then what we can do is change it. Instead of three weeks on, one week off, do it two weeks on, two weeks off. So, play a little bit with the frequency and see if that helps. And, yeah, it's important.

Some patients also I've seen this too that they are on Revlimid continuously, like no breaks, like every single day. And even though some of the studies that look at Revlimid maintenance that's what they do, in my experience, getting that week break helps. Like it gives your body a little chance at least to heal. So that's also things to consider.

And if none of that works, then I would say you need to discuss with your doctor and see if there's any other treatment alternative. Really it depends on what stage of the disease you are.

**Lizette Figueroa-Rivera, MA**

Thank you. And our next question comes from James. James is asking, "What role does individualized genomic testing and analysis play in deciding which myeloma treatment option would be the most effective and/or the most risky?"
Melissa Alsina, MD

That is an excellent question. And there are studies ongoing looking exactly at that and trying to predict based on the genomic way what would be the best treatment for a patient and so on. But that is not clinically available yet so it's not something that we can apply clinically except for a few cases. Like there's some mutations in particular that we know there's a drug that we can target specifically. For example, there's a mutation that is seen in lung cancer that is called BRAF (v-raf murine sarcoma viral oncogene homolog B1), and if the patient has it, then there's a drug to target that. There's another mutation, it's not a mutation, it's a translocation from chromosome 11 and 14, and there is a drug that is called venetoclax that is approved to treat chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML). But if the patient with myeloma has that translocation, that venetoclax works fantastically. We can use it in combination with a proteasome inhibitor like Velcade or with Darzalex and with really good results. And we also know that patients that have high-risk myeloma, like translocation 4;14, those patients benefit from getting proteasome inhibitors like Velcade-Kyprolis and so on. So, we have a few things that can help not universally because not all patients have those abnormalities. And, again, the genomic studies who try to predict response to one agent versus the other, those are ongoing but they're not prime time yet to be able to apply clinically.

Lizette Figueroa-Rivera, MA

Thank you. And the next question is coming from Sanetra. She's asking, "Has there been any further research on monoclonal gammopathy of undetermined significance, or MGUS, and its progression to multiple myeloma? Do other conditions such as autoimmune disease increase the chances of MGUS developing into myeloma?"

Melissa Alsina, MD

No. So, there have been a lot of research in MGUS because MGUS is a relatively common condition as opposed to myeloma. It's like almost one in 12% chance that someone up to age 80, for example, would have that condition. And thousands of patients have been studied with that condition. And what has been shown is that, yeah, it's more commonly in patients that have autoimmune diseases. However, your autoimmune disease doesn't make your MGUS progress quicker. And the risk of progression is only 1% per year, but it's a cumulative progression, right, so, I don't know, if you're diagnosed at age 70 and you live until 90, then you have a 20% chance of developing myeloma for MGUS. But chances are that you will not develop myeloma, and we follow these patients by doing labs like once a year or every six months to make sure everything is stable.

Lizette Figueroa-Rivera, MA

Thank you. and the next question from Natalia asks, "If my husband is currently on dialysis due to kidney problems, can he still get treatment for myeloma?"
Melissa Alsina, MD

Oh absolutely. Absolutely. So, it depends on what stage we are of the disease, but the majority of the drugs that we have approved for myeloma we can give in patients with kidney failure. Immunomodulatory drugs, especially Revlimid which is metabolized in the kidney, we can still give it, but we have to give reduced doses. For example, if a patient is on dialysis, we give like 5 milligrams three times a week after dialysis. But other drugs like proteasome inhibitors, like Velcade, Kyprolis, steroids, Darzalex, all those drugs can be given in patients with kidney failure even the new drugs, this antibody Blenrep that we talk about. Transplants, we can do transplants in patients with myeloma that are on dialysis or in kidney failure. And CAR T and these other new drugs, the immunotherapies that I talk about, like the BiTEs, we don’t know. Those have not been studied, but I'm pretty sure that when CAR T is approved, hopefully in a month, then we'll start evaluating if we can do this in patients with renal failure.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from our telephone audience, please.

Operator

Our next call is from Mary from Texas. Mary, please state your question. Your line is now live.

Mary from Texas

Yes, good afternoon. A lot of my questions have been answered that I was concerned about. It was with the vaccine and having the myeloma. My other thing is why would your ankles and feet swell up? Would that be from the Velcade or from the Revlimid?

Melissa Alsina, MD

Hi Mary, I hope you're doing okay with all your bad weather in Texas. So, that is a very nonspecific symptom that it could be related to many things. In general, the most common drug that we use for myeloma that causes the swelling and the fluid retention is the steroids, the dexamethasone. The Revlimid and the Pomalyst, you know, if you develop, for example, swelling in just one leg, then you have to be evaluated for a blood clot because Revlimid and Pomalyst increase the risk of developing blood clots. The Velcade usually don't cause any swelling, so it's usually the dex. And then the other possibility could be sometimes patients with myeloma the kidneys are affected and you're losing normal protein in the urine; and when that happens, that causes swelling of your extremities so that could be the other cause. But, there are many other causes for swelling of the legs, including high blood pressure, peripheral venous insufficiency, uncontrolled diabetes, other medications that you might be taking, so it's hard to know exactly what the cause is without seeing you but it's something to discuss with your doctor, I think, in more detail.
Lizette Figueroa-Rivera, MA

Thank you. And Patricia is asking if a second stem cell transplant is suggested even if the present treatment is working fairly well.

Melissa Alsina, MD

So, the second transplant, I mean second transplants can be done safely, but I think nowadays because we have so many other treatments that we can do, including CAR T coming up, the use of a second transplant for when the disease gets active again after the first transplant, it has been used less and less and less. We're still collecting enough stem cells for two transplants, but we are not doing second transplants hardly ever, not because we cannot do them. They can be done but just because there is a not a need for it because there are other treatment alternatives that perhaps are even better than a second transplant.

The other thing that, you know, someone that is doing a second transplant the expected benefit would be half of whatever you had with the first transplant. So, let's say you had a transplant, and you had a remission of ten years. Then the second transplant, more than likely, would last five years, so it's a little bit more worth it in a case like that as opposed to someone who had a transplant and relapsed within two years. Then doing a second transplant is probably not worth is because there are other treatments that can cause responses even longer than that.

Lizette Figueroa-Rivera, MA

Thank you. And Mary is asking about the progress being made finding therapies specifically targeting patients with the 17p deletion.

Melissa Alsina, MD

Wow, that is an excellent question. So, 17p deletion, for those of you that are not aware, it means patients have a deletion of part of chromosome 17. And the deletion happens on a place where there's a gene that is a tumor suppressor gene. So that's a mechanism that your body has to control the growth of the cancer, right. And then that gene is gone so now your cancer can grow. And that is probably the gene that most significantly affects the myeloma prognosis. And no, unfortunately, we do not have any medication that targets that gene specifically in myeloma. There is a medication that is in clinical trials that is being looked at in patients with acute leukemia that can target that 17p deletion or myelodysplastic syndrome (MDS) but not in myeloma. But it's one of the most challenging scenarios that we face when we treat the myeloma patients.

Lizette Figueroa-Rivera, MA

Thank you. And our next question comes from Cathy. Cathy asks, "What are the issues with taking my medication late due to things like shipping problems, etc.?"
Melissa Alsina, MD

You usually want to take these medications on the schedule that you're supposed to take them. But I think you need to talk to your doctor or the specialty pharmacy and try to see if they can find a way of getting it to you on time. Unfortunately, there's not a secret solution for that, you know, a magic solution for that except trying to reach out to those people that are supposed to get you the medication and see if there's anything they can do but certainly it would be important. I mean I would say if you take the medication one or two days late, then it doesn't matter. But if you're taking the medication weeks late, then that is an issue.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from the telephone audience, please.

Operator

Our next call is from Richard from North Carolina. Richard, please state your question. Your line is now live.

Richard from North Carolina

Yeah, I just was wondering if you knew anything about the measles virus therapy and, also, was wondering where you practice.

Melissa Alsina, MD

Yeah. So, you know, the measles virus that was an old study. I don't even remember when it was, but it was a long time, I mean like many years ago that it seemed like it was causing the myeloma to get active and some of the measles virus sequence was in the myeloma cells. But that research was not confirmed, so that is something that failed, that it was not shown to be true that that was real and that using the measles vaccine could play any role in the treatment of myeloma.

What was the second question you said?

Lizette Figueroa-Rivera, MA

Where do you practice?
Melissa Alsina, MD

Oh, I practice at Moffit Cancer Center, which is a cancer center over in Tampa, Florida.

Lizette Figueroa-Rivera, MA

Thank you. And the next question comes from Harold. Harold is asking, "What are the alternatives to control back pain resulting from the myeloma?" Currently is on oxycodone.

Melissa Alsina, MD

So, it depends on what's causing the pain, right, but a very common cause of back pain with myeloma are compression fractures which it means I mean the vertebra should be like a square, but they can cross on each other or a vertebra can cross on itself because the bone gets very weak from the myeloma. And that is called a compression fracture and that can cause a lot of pain. So, there's a procedure that is called kyphoplasty where they put a needle in the vertebra in a little balloon and then cement to expand the vertebra and sort of release that pressure. And that is very helpful with the pain and it's a relatively simple procedure, like, one-day surgery and so on. Physical therapy sometimes can help with that depending on what area and there is sometimes also nerve blocks depending, again, on what's causing the problem. Usually, we're trying to assess that. We will do an MRI (magnetic resonance imaging) of the spine and then the two people that could help you probably the most is a spine surgeon, which could be a neurosurgeon or orthopedic surgeon to see if there's anything surgically that they can do to help. And the other person that can help with that would be an interventional pain specialist. These are usually anesthesiologists that work in pain control. They're good because they can do both things; they can treat you medically for the pain, but they can also do intervention like a nerve block or other modalities that could help that are not just oxycodone.

Lizette Figueroa-Rivera, MA

Thank you. And we'll take the next question from the telephone audience, please.

Operator

Our next call is from Dee from Texas. Dee, please state your question. Your line is now live.

Dee from Texas

For the MRD versus if you have a diagnosis of a very good partial remission, where does that fall in the vocabulary of the MRD terminology?
Melissa Alsina, MD

Yeah. So, when we have early response in myeloma, we look at the protein made by the cancer cells, what we call the monoclonal protein or the M spike. And we say that protein goes away completely, and the bone marrow is normal, then that would be a complete remission. If that protein goes down by 90%, that would be a VGPR, a very good partial response. If that protein goes down by more than 50%, that would be a partial response (PR), and so on. So, you could have a patient that is in complete remission, the bone marrow is clean and then you look back for minimal residual disease and that could be positive or negative. And if we have a patient that is in VGPR. It means the protein has reduced by more than 90%, so there's still a little bit of monoclonal protein, but the bone marrow could be normal. No myeloma in the bone marrow and it could be MRD negative as well. So, you could have VGPR and be MRD negative. And the reason for that is that, you know, the cancer cells are gone but the half-life of that abnormal protein is very long so it can just stay in your body and then with time, it can go away.

And we're seeing that a lot now with CAR T because CAR T is like these CAR T cells, you know, they go in the bone marrow, they kill all the myeloma that is there but then months later patients are MRD negative. You don't see any myeloma in marrow, but you still see a very tiny M spike in the blood. And with time, that goes away. So MRD means minimal residual disease. It's a deeper response. It's a test that can detect one in a million cancer cells. And, yes, you can be minimal residual disease negative but have a VGPR as opposed to a complete remission. I hope I answered your question.

Lizette Figueroa-Rivera, MA

Thank you. And our last question today. Bonnie, asks, "My stem cell transplant was allogeneic in May of 2009. I was on maintenance dose of Revlimid until December of 2019 and was told by my oncologist I could be considered cured. What are your thoughts?"

Melissa Alsina, MD

Well, you know, it definitely could be true. I mean allogeneic transplant were used and those are getting a transplant from a donor, getting cells from a donor as opposed to the own patient cells. So allogeneic transplants we started doing those probably 20 years ago or more and the problem in Italy was that the mortality associated to the transplant was very high, so we stopped doing them. Then they were done again differently and there were some good results, but bottom line was that only a very few number of patients were cured. And because allogeneic transplants are more risky with more risk of having like the cells from the donor attack your cells and get this graft versus host disease (GVHD) syndrome that could be very complicated, we were not doing them as much. And then we're having other new treatments in myeloma, better treatments. So bottom line is that all these things make transplant, allogenic transplant go away.

We tried to do a study, a national study a few years ago, and the study had to be closed because we were not able to accrue any patients, and it was a national study. But some of those patients that had an allotransplant ten years ago or more, some of those patients are doing well and are in remission
like you are. So, yeah, I would agree that it's probably true. Usually when we do allotransplant, we do not give any maintenance. I actually did a study where we did Revlimid maintenance after allotransplant, and it didn't work very, very well because it could induce graft-versus-host disease.

So, yeah, I mean there are not many patients. There are a handful of patients that have received an allotransplant many, many years ago and they're without areas of disease and potentially cured.

Lizette Figueroa-Rivera, MA

Well thank you, Bonnie, for that question, and thank you all for your questions. And thank you, Dr. Alsina, for your continued dedication to our patients.

CLOSING REMARKS

Lizette Figueroa-Rivera, MA

And if we weren't able to get to your question today, please call our Leukemia & Lymphoma Society Information Specialists at 1-800-955-4572. Information Specialists are available to speak with you from 9AM to 9PM Eastern Time or you can reach us by email at Infocenter@LLS.org. Also, patients, as well as caregivers, can schedule a free personalized nutrition consult with our dieticians at lls.org/consult.
Again, please note that we will post a transcript on our website for this program in about three or four weeks and that will be on lls.org/programs. And the slides are already on our website.

LLS offers a variety of education and support resources, including online chats which are free, live forums that are moderated by oncology social workers. We also offer free education videos and podcasts.

The Leukemia & Lymphoma Society offers programs to help individuals with blood cancer. For more information, you can visit lls.org/finances, and you can order free materials by visiting lls.org/booklets.

Please note that continuing education credits is not being offered for this program.
Again, we would like to acknowledge and thank Bristol Myers Squibb, Genentech & Biogen, GlaxoSmithKline and Takeda Oncology for their support of this program.

And thank you so much, Dr. Alsina, for sharing your knowledge with us today and to all of the patients, caregivers and professionals participating in today's program. And on behalf of The Leukemia & Lymphoma Society, thanks so much for sharing your time with us. Good-bye, and we wish you well.