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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Patients as Partners: Frontline Management of Multiple Myeloma

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Chapter 1: Latest Guidelines and New Advances in Frontline Treatment

Dr. Costello:
Patients newly diagnosed with multiple myeloma are often experiencing various symptoms, including pain and fatigue. Fortunately, amazing strides have been made in treatments that are improving our patients’ quality of life. This is CME on ReachMD, and I’m Dr. Caitlin Costello.

Dr. Vij:
And I’m Dr. Ravi Vij.

Dr. Costello:
Hi, Ravi. Can you tell us a little bit about recent advances for the management of our patients with newly diagnosed multiple myeloma?

Dr. Vij:
We have recently seen tremendous advances in the treatment of our patients with multiple myeloma. Firstline therapy continues to evolve, both for transplant eligible and transplant ineligible patients.

What we have seen over the last year, year and a half, in the United States is a move towards the four-drug regimen of daratumumab, with pertuzumab, lenalidomide, dexamethasone in patients undergoing stem cell transplantation. This is based on the GRIFFIN study, that randomized patients pre-transplant to that four-drug regimen versus the prior standard of care, three-drug regimen of bortezomib, lenalidomide, and dexamethasone. In this trial, patients post-transplant who got four drugs got lenalidomide and daratumumab for maintenance, and those that got three drugs, got lenalidomide alone.

Much higher rates of depth of response including MRD negativity, were seen in this four-drug regimen approach. This is something that is expected in the future to lead to better progression-free survival and possibly overall survival.

The use of a carfilzomib in induction therapy of transplant eligible patients continues to be explored as well. We have seen the regimen of Kyprolis, lenalidomide, and dexamethasone studied by numerous groups. The U.S. experience by Dr. _(9:09) was followed by a trial that was done by the IFM group that showed again high rates of MRD negativity in patients who get Kyprolis-based induction followed by maintenance therapy.

The data on Kyprolis as a four-drug combo also is now evolving. The FORTE study, which was a three-drug regimen did, in a randomized trial, show superiority with when paired with transplantation compared to a regimen where Kyprolis, lenalidomide, and

dexamethasone was given without transplant. Building on that, trying to incorporate the use of four-drug regimens, including daratumumab, Kyprolis, lenalidomide, and dexamethasone into the mix is a strategy that is starting to pay dividends.

The MASTER study that was published recently in a major academic journal showed that the four-drug regimen produces unparalleled rates of remission, including MRD negativity at 10 to the power of -6. This trial explored using MRD as an endpoint to decide on length of therapy as well.

At the recent ASCO meeting, the ATLAS study that showed that Kyprolis with lenalidomide as maintenance strategy post-transplant, had severe outcomes that compared to lenalidomide maintenance alone. And this again, is something that was seen earlier in the FORTE study, as well.

At the ASCO meeting, we also had a French study, looking at the four-drug regimen of daratumumab, with Kyprolis, lenalidomide, and dexamethasone presented with impressive rates of depth of response.

So, I think that four-drug regimens are something that are going to continue to be becoming more popular for our patients.

In the non-transplant eligible population, the three-drug regimen of daratumumab with lenalidomide and dexamethasone with longer-term follow-up is producing progression-free survivals of approximately 5 years which is unparalleled. In the future, we will likely see four-drug regimens even for the non-transplant eligible patient population.

In this population, some people still give bortezomib, lenalidomide, and dexamethasone in a dose-reduced manner. This is something that again is one of individual preference. The use of a four-drug regimen of elotuzumab with bortezomib, lenalidomide, and dexamethasone, however, cannot at this time be something that we can endorse since a study done by the SWOG cooperative group in high-risk patients did not show any advantage compared to a three-drug standard of lenalidomide, bortezomib, and dexamethasone alone.

Dr. Costello:
Thank you, Ravi. It really feels like an embarrassment of riches sometimes, when it comes to the management of newly diagnosed multiple myeloma. There are really just so many great options and novel combinations, whether it's doublets, triplets or quadruplets, as you mentioned.

It can get a little confusing, however, and it really is up to us as clinicians to try and identify the most ideal combination for every individual patient. And that may require looking at patients' biology of their disease, patients' comorbidities, patients' psychosocial and their support system, to really try and personalize, to some degree, the best treatments that we can offer, to both maximize effectiveness but also to minimize toxicity and complications. And there have been so many things that have made treatment even more easy, let's say, for our patients, where now we have the option for subcutaneous formulation of daratumumab, which can really be much more beneficial and convenient for patients, infusion centers, physicians, nursing staff alike. There are options for all oral combinations just the same, which are helpful for patients who may have limited access to infusion centers. So, all in all, we have a really wonderful number of therapies that are available to us that are extremely effective. It's just a matter, I think, and up to us, of choosing what is perfect for every individual patient. So, this has been great. Before we wrap up, Ravi, can you provide us with one key takeaway from this chapter?

Dr. Vij:
The key takeaway is that four-drug regimens are now becoming the de facto standard of care for patients who are transplant eligible. In the future, these are likely to even become standards for non-transplant eligible patients as well.

Dr. Costello:
Thank you. In Chapter 2, we'll be evaluating new advances in treatment decision-making. Stay tuned.

Chapter 2: Evaluating New Advances in Decision-Making

Dr. Vij:
Welcome back. In the first chapter, we talked about the current guidelines for front-line treatment of multiple myeloma. In this section, we are going to talk about what is the optimal depth and duration of treatment. Caitlin, can you tell us how you would aim for deep responses in patients with myeloma these days?

Dr. Costello:
Thank you, Ravi. That is such a great, relevant question right now, is that we have so many options for treatment, but our goal really should be the same. As clinical trials have evolved over the last many years, we have seen this evolution from endpoints requiring, you know, overall response rates to improved for progression-free survival. However, more recently, we're understanding the importance of

minimal residual disease, and how that could potentially reflect the same prior endpoints, including how long patients may end up remaining in remission, and presumably, then, would have improved overall survival. So as overall response rates have historically helped us in clinical trials understand the effectiveness of the drugs, what we now understand from clinical trials is the evaluation and quantification of minimal residual disease, and the importance of getting to a minimal residual disease state is really relevant in terms of understanding how long these patients should stay on therapy, how long these patients may require to stay on therapy, in order to improve their overall survival, but also may eventually have implications for when we may be able to stop therapy. And so, these patients, importantly, are evaluated for their ongoing bone marrow biopsies, as a means to understand have they achieved the deepest response possible, so that we, therefore, can make educated decisions and prognostic decisions to understand how to further continue their therapy or potentially stop.

Dr. Vij:
I agree, and the duration of therapy certainly is something that has also evolved with time. We used to have a paradigm of start and stop after maximal response, and resume at progression. Increasingly, it is one of continuous therapy. For those that are transplant-eligible, we give them four to six cycles and after they've had at least a partial response or better, move them to transplant. Post-transplant, we continue maintenance dose time of disease progression, though some patients can't tolerate it and do have to stop treatment early. For those who are not transplant-eligible, once again we do try to, after a period of induction, reduce the intensity of the treatment, but continuous therapy with one or more drugs, depending on the regimen used, is what we tend to practice today. So, this has been great, Caitlin. So before we wrap up, would you give us some key takeaways from this section?

Dr. Costello:
Sure, Ravi. I think it's become clear that depth of response matters, and eventually this may provide us information to understand how we can adjust patient therapies, whether to continue or potentially to stop in the future.

Dr. Vij:
In Chapter 3, we will shift gears and look at important considerations from the patient's point of view. Stay tuned.

Dr. Costello:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Caitlin Costello, and here with me today is Dr. Ravi Vij. We're discussing the front-line management of patients with newly diagnosed multiple myeloma.

Chapter 3: Patient Educational Video

Dr. Vij:
Welcome. In Chapter 2, we discussed the appropriate goals and duration of treatment. Now I will hand it over to Dr. Costello to tell patients how they should approach their initial appointment with their oncologist.

Dr. Costello:
Hi, I'm Dr. Caitlin Costello, a myeloma specialist at the University of California at San Diego. Now, we know that getting a diagnosis of any cancer can be a very overwhelming situation, and I hope that if you have been diagnosed with multiple myeloma recently, that you will find that this next update will be very helpful in answering some of your questions, or to prepare you for what to expect with your upcoming consultation with your oncologist. It is important to prepare for your appointment with your oncologist, so you know what you're going to ask, and know what you hope to leave with, in terms of answers to many of your questions. I think it is most critical for when you start the conversation, to understand from your oncologist exactly what it is that they know about your multiple myeloma.

What kind of multiple myeloma do I have? What stage of multiple myeloma do I have? What kind of treatments are available to me, in order to improve my cancer and make me feel better?

You and your oncologist now make up an important team, where we can understand what the best treatments are for you, based on your specific form of multiple myeloma, based on any other medical conditions that you have had, and choose something that is particularly personalized, to help improve your specific situation. It is important to ask about the treatments that you will be receiving.

What would you expect them to do, in terms of side effects, or how would they expect them to work in your particular scenario? It's important to understand that treatments can come in the form of pills, or shots, or infusions, and can be very convenient in the means of which they are administered, without involving hair loss, or oftentimes significant nausea and vomiting, that we frequently associate with chemotherapy. And so, as you are receiving these treatments, it's also important to understand from your oncologist how they will be able to assess how the treatment is working. Do I need blood tests, or do I need pictures of my bones, to understand how the myeloma has affected them, or how they are getting stronger?

Most importantly, it is critical that you remain very open and honest with your oncologist about any side effects that you may be

experiencing from medications. We always like to say, we have lots of tricks up our sleeve to help you feel better, but we can't help if we don't know. So it's important to ask what to expect, as far as side effects are with the individual treatment that your oncologist has prescribed, and make sure that you are monitoring those along the way, so you can provide the feedback that may help your oncologist understand how to make adjustments, to make the treatment regimen more tolerable and still maintain its effectiveness.

I know this can be a scary time, however, it's important to realize that the treatment of multiple myeloma has really allowed for just significant improvements in patients' quality of life most importantly, but also to understand that patients can live for a very long time with this, sometimes considered more chronic cancer now.

Dr. Vij:
Thank you, Dr. Costello, for your excellent guidance. I'm sure patients will find this extremely useful during their consultation. That is all the time we have today. Thank you very much, Caitlin, for joining us today.

Dr. Costello:
Thank you, Dr. Vij. It's been a pleasure being here with you.

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