Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/keeping-pace-in-hematologic-malignancies-optimizing-treatment-selection-in-relapsed-or-refractory-multiple-myeloma/13823/

Released: 06/30/2022
Valid until: 06/30/2023
Time needed to complete: 15 minutes

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

Keeping Pace in Hematologic Malignancies: Optimizing Treatment Selection in Relapsed or Refractory Multiple Myeloma

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Keeping Pace in Hematologic Malignancies: Optimizing Treatment Selection in Relapsed or Refractory Multiple Myeloma” is provided by Prova Education.
Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Krishnan:
Despite rapid advances in therapeutic options, multiple myeloma remains incurable. Most patients inevitably relapse. And it's a very crowded space in relapsed myeloma, no simple algorithm to select the best therapy. So how do we incorporate the most current data to develop an individualized treatment plan for these patients? This is CME on ReachMD, and I'm Dr. Amrita Krishnan.

Dr. Gertz:
And I'm Dr. Morie Gertz. There are now several combination regimens consisting of proteasome inhibitors, immunomodulatory agents, monoclonal antibodies, and novel targeted therapies. Let's consider several case scenarios and discuss how we're translating the latest clinical data into practice.

So let's start with a 62-year-old male with multiple myeloma, back pain. MRI confirms compression fractures and lytic lesions. Laboratory evaluation shows 40% bone marrow plasma cells, and the patient has standard risk FISH. Beta-2 microglobulin is 4.7 with an albumin of 4 grams international stage 2. LDH is normal. The patient initially is treated with bortezomib, lenalidomide, and dexamethasone VRD followed by a single autologous stem cell transplant, melphalan 200. The patient begins lenalidomide maintenance therapy 10 milligrams, 3 weeks out 4, on day 100 and sustains a biochemical relapse without symptoms 27 months later. What do we do now?

Dr. Krishnan:
This is probably one of our most common scenarios in regards to a patient on len maintenance, now progressing. Even though you said he was standard risk, Morie, I do think he's somewhat of a higher risk given his median progression-free survival after transplant was relatively short. This patient has a plethora of options. Some of this is a really individualized discussion with the patient in terms of some of his preferences as well. Some of the comorbidities that maybe we'll get into of the different choices, I would say at our center right now, we would definitely consider the use of an anti-CD38 monoclonal antibody. And it really would be the partner to that, that would be under discussion with the patient, i.e., should we combine with a proteasome inhibitor, either bortezomib or carfilzomib. I am pretty impressed with the data from CANDOR with daratumumab plus carfilzomib and dexamethasone with a PFS of 28.6 months in that triplet arm. Similar, we have some impressive data with isatuximab plus carfilzomib and dex. Here the median PFS in the IKEMA trial hasn't been reached. So again, carfilzomib plus an anti-CD38 antibody is a very good combination, combining a different IMiD, so pomalidomide based on the APOLLO trial, or of dara plus pom, dex, there, a PFS of 12.4 months or the ICARIA trial which is pretty similar isa, pom, dex PFS 11.5 months.

I think both those options are very reasonable. And it becomes a question of some toxicities, which I think you know, I'll let you comment

on it, when you discuss it with patients.

Dr. Gertz:
I agree with all of those therapeutic options, but when we're truly trying to individualize therapy for a patient, we need to take into account the therapy-related adverse events. Obviously, with the long survivals we're seeing now with multiple myeloma, we need to be cognizant of irreversible toxicities. Things that could be considered would be, does the patient have preexisting peripheral neuropathy that would make the use of bortezomib, a more difficult choice. What about the risks of venous thromboembolism associated with all the immunomodulatory drugs? Will that mean long-term anticoagulation with a novel anticoagulant? Does the patient have any relative contraindications? Long-term myelosuppression with the long-term use of maintenance therapies and induction with the increased risk of infection and transfusion dependency should be considered. For agents such as belantamab, there's the very unique corneal toxicity that occurs, that can often force patients off drug. And if carfilzomib is selected, because it is a highly active agent, the issue of the cardiac signal. How much fluid do we give before and after the infusion? Does the patient have pre-existing hypertension? Or does the patient have a reduced ejection fraction that might increase the side effects associated with cardiac toxicity?

Dr. Krishnan:
Morie, if you want to comment on the infection risk a little bit more because I was struck, in CANDOR, for example, in older patients over 65 have the high percentage of significant infectious events, including fatal adverse events.

Dr. Gertz:
That's a very important comment. There's no question that all anti-CD38 antibodies suppress the immune response. There's a much higher risk of significant infections. In the BELLINI trial that used venetoclax, there was a higher risk of infectious death. And so, issues are is it appropriate to consider long-term antibiotic prophylaxis, become a relevant issue. And in patients who are receiving daratumumab and isatuximab, there's demonstrated blunted responses to COVID vaccination.

Dr. Krishnan:
I think that adds another layer of complexity to our treatment decision for these patients.

For those of you just tuning in, you're listening to CME on ReachMD. I'm Dr. Amrita Krishnan, and here with me today is Dr. Morie Gertz, and we're discussing how best to treat patients with relapsed refractory multiple myeloma given these many novel combinations, many new therapies that are rapidly being introduced into the treatment landscape.

Okay, let's turn to a different scenario. A transplant ineligible patient. This is a 77-year-old who presented with fatigue, was found to be anemic, hemoglobin of 8.8, also had significant renal insufficiency, a creatinine of 2.1. The patient was treated with daratumumab, lenalidomide, and dex, did well for about 19 months and then had a fairly quick progression with a doubling of serum immunoglobulin free light chains. At this point, the patient was on monthly dara and a len dose of 10 milligrams. Now what do we do?

Dr. Gertz:
This is also a very common problem, a patient who is relapsing on dual maintenance therapy. And in my experience, although the published data is not very extensive, is that for example, escalating the lenalidomide dose from 10 milligrams back to 25 milligrams, or increasing the frequency of daratumumab infusions has not been effective in my practice. I would consider this patient completely refractory to an anti-CD38, and to lenalidomide.

In patients like this, I would certainly be repeating the bone marrow biopsies. I could get FISH, because if this patient has the 11;14 translocation, this patient will be a high expressor of BCL2 and venetoclax, often at a reduced dose of 400 milligrams, will be effective. But if the patient is, as likely, not going to carry that, this is a patient where I normally go directly to carfilzomib, pomalidomide, dexamethasone, or carfilzomib cyclophosphamide, dexamethasone, as this patient is alkylating agent naive, and has not been exposed to melphalan as part of a transplant, an alkylating agent can be quite effective. Nonetheless, we have to be cognizant again, a 77-year-old, will there be cardiac complications with carfilzomib? How well will the patient tolerate pomalidomide in terms of maintaining their blood counts, so they can get therapeutically effective doses? What's the appropriate dexamethasone dose for a patient that is 78 years old? And then the question comes up, is early initiation of selinexor, a consideration using the newly described suppressive antiemetic regimens that are used to prevent the weight loss so commonly seen? Finally, of course, early introduction of belantamab. There are trials looking at belantamab combined with selinexor. We have both novel agents carfilzomib, pom; as well as really new agents such as the belantamab, selinexor.

Amitra, what if this patient relapses multiple times?

Dr. Krishnan:
So for the multiple relapse patients, especially those four or more prior lines of therapy, we are fortunate to have new options. So we have approved options that includes the antibody drug conjugate, belantamab, mafodotin, CAR T-cells. Also approved in this space,

though in this patient the CAR T discussion, I think would be a little bit more challenging based on the renal insufficiency in this patient.

When is a patient not transplant eligible but CAR T eligible? There is data from CARTITUDE and KarMMa in patients over the age of 65. The PFS seems comparable. We do know older patients have probably higher risk in terms of neurologic toxicities, for example. And we don't have data in patients with this degree of renal insufficiency but certainly in the real-world setting we are doing it in patients with some degree of renal impairment. I wouldn't rule out CAR T, but I'd be a little bit more cautious in this patient.

When is a patient not transplant eligible but CAR T eligible? There is data from CARTITUDE and KarMMa in patients over the age of 65. The PFS seems comparable. We do know older patients have probably higher risk in terms of neurologic toxicities, for example. And we don't have data in patients with this degree of renal insufficiency but certainly in the real-world setting we are doing it in patients with some degree of renal impairment. I wouldn't rule out CAR T, but I'd be a little bit more cautious in this patient.

And then we also look to some unapproved but new agents on the horizon, specifically the bispecifics. And those can be BCMA-targeting, specifically teclistamab, but also other targeting agents, such as the FCR5 targeting agents, cevostamab, and the GPRC5D-targeting bispecific, talquetamab. And again, they've all shown a lot of promise in patients with advanced disease, at least a median of five prior regimens.

Dr. Gertz:
Thank you, Amitra. Finally, let's discuss a patient with high-risk multiple myeloma. A 63-year-old woman presented with 70% bone marrow plasma cells, and a PET scan showed extramedullary disease in the liver, biopsy proven, with deletion 17p and translocation 4;14. This patient was initially treated with daratumumab, carfilzomib, lenalidomide, dexamethasone followed by tandem stem cell transplant and two-drug maintenance with daratumumab and lenalidomide. Not surprisingly, she relapses at 7 months of maintenance therapy, and moves on to selinexor, pomalidomide, dexamethasone, relapses within 6 months and has a brief response to parentally-administrated cyclophosphamide. So what can we use for a multiple relapse high-risk patient, Amitra?

Dr. Krishnan:
Unfortunately, this is probably an all-too-common scenario, young patient with incredibly aggressive disease, who got the best drugs that we had to offer up front as induction and even tandem. This is really the place where I would look at some of the emerging therapies and look to bispecifics, look to the use of early CAR T-cells. And there are some trials looking at CAR T in patients with one to three prior relapses. And looking at other new targeting bispecifics because this patient has progressed through the best available drugs that we have. And I think we need to find newer options. And I would look to immunotherapy options for this patient.

Dr. Gertz:
I agree with that. One thing I was so excited about was the MajesTEC study that looked at teclistamab, heavily pretreated patients 65% overall response rate and cytokine release syndrome was not seen. And so, this whole concept of off-the-shelf BiTE therapy that can be repeatedly administered is very exciting, recognizing that these patients have exotic infectious complications.

Dr. Krishnan:
This has been a fascinating, enlightening conversation. Before we wrap up, Morie, can you share your one take-home message with this audience?

Dr. Gertz:
Thank you. With the growing variety of combination therapies being evaluated, it's critical to be confident in individualized therapy for patients with relapsed myeloma, including the potential toxicities of the agent selected.

Dr. Krishnan:
My final take-home message is to echo what Morie said—that really it's important to balance efficacy and toxicity to achieve optimal outcome for our patients.

Unfortunately, that's all the time we have today. So I want to thank our audience for listening and thank you, Dr. Morie Gertz, for joining me and sharing your valuable insights. It was great speaking with you today.

Dr. Gertz:
Thank you very much and goodbye.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education.

To receive your free CME credit, or to download this activity, go to ReachMD.com/ Prova. Thank you for listening.