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Released: 08/21/2026
Valid until: 08/21/2027
Time needed to complete: 38m

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# Case Consult: Implementing Anti-CD38–Based Frontline Regimens in Transplant-Ineligible Patients

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**Dr. Callander:**
Welcome. This is CE with GLC, and I'm Dr. Natalie Callander, and I'm here with my colleague Saad Usmani. We're going to have him start with a discussion of a case.

**Dr. Usmani:**
Thank you so much, Dr. Callander. I'm Dr. Saad Usmani. Let's discuss with a case.

We have a 73-year-old Caucasian man who presented to his primary care physician with increasing back pain which was not getting better with conservative measures. This is many times the way that our multiple myeloma patients present. They had an X-ray of the lumbar spine, which showed numerous lytic lesions that prompted a referral to a hematologist-oncologist for further workup.

I do want to highlight that the patient does have a history of coronary artery disease with compensated CHF, with the ejection fraction being 45%. They do have type 2 diabetes with mild sensory neuropathy in their feet, and they do have renal insufficiency as well. So their ECOG performance status at baseline at best is around 2.

When we looked at their labs, their hemoglobin was 9.7. Their creatinine had crept up from the baseline of 0.9 to 2.3 mg/dL, and their serum protein and calcium levels. Serum protein was normal, but calcium was mildly elevated. Albumin was lower, and the beta-2 microglobulin was 5.6.

Looking at the protein studies, it looked like they had lambda light chains on immunofixation on the SPEP IFE, and the serum kappa light chains were 17.5, whereas the lambda light chains were elevated at 244.3 mg/dL. So, bone marrow biopsy was done, showing 45% plasma cells. They were lambda light chain restricted. Again, this patient appeared to be standard risk on the FISH profiling with translocation 11;14. The PET/CT did show several lytic lesions, three FDG-avid lesions in particular, with the SUVmax being 9.1.

So they get diagnosed with Revised ISS stage II lambda light chain multiple myeloma. They do appear to have certain comorbid disease at baseline.

So, Dr. Callander, what would your thoughts be around picking an anti-CD38-based triplet versus a quadruplet for this transplant

ineligible patient?

**Dr. Callander:**
I think that's a great question, and I think this case is very typical for the kinds of patients we see. We know that about 40% of the patients we're going to see with newly diagnosed myeloma are over age 75, and this gentleman in particular has a lot of comorbidities.

So I think I'm sure as you do as well, I do consider quadruplet therapy for most patients if I think that they are fit enough. But there is some subjectivity, and of course you want to look at not only just things that are I think fairly obvious like age and frailty, but I think you also want to look at some other practical considerations. How hard is it for the patient to get to the clinic for treatment? So if you're going to recommend that the person is coming in once a week, is that going to be feasible? I think those are issues. Do they have a good caregiver?

I think that helps you decide whether you're going to add some degree of complexity by moving to a quadruplet, and there certainly are patients in whom I think a triplet is appropriate. But I'd be interested in your thoughts as well.

**Dr. Usmani:**
And I think you bring up very important points. I think in addition to frailty and comorbidity considerations, there are patient preferences to be discussed. And for older patients, we have to think about their social support structure and kind of build that into uh our planning as well.

Many times, because they have multiple comorbidities, we want to work closely with their primary care physicians, with even geriatric services, to make sure we're optimizing their other medical problems in addition to multiple myeloma. And we do have to consider a very holistic view in caring for these patients.

The goals of care, of course, are to get their disease under control and offer them the best initial remission period. But it's a balancing act, so you have to pay attention to so many other things.

**Dr. Callander:**
Right. And how do you address concerns that patients have if you say I'm going to give you a four-drug regimen? What do you tell patients about adding in that fourth drug?

**Dr. Usmani:**
Yeah, I think it's important if someone is coming in with a higher disease burden or biologically high-risk disease where it would be a good idea to perhaps get the disease under quicker control and add the proteasome inhibitor. You have to do this in a dose-attenuated fashion, and also talk to them about logistics, you have to prep them for initial potential side effects because the sooner we learn about them, the sooner we can act by stopping that drug and even modifying the dosing further. I think the eventual goal is you want to get them into good disease control in the safest fashion possible.

And again I also mentioned the logistic concerns. I think having good social support is important. So it's not just about educating the patient, but also educating the caregiver.

Historically, if we go back to the triplet era where initially RVd was the initial induction or preferred induction of choice, we remember Dr. Raje, who looked at RVd Lite, where she actually did a dose-attenuated regimen, which got the older patients into a similar kind of response and progression-free survival as a more intensive RVd induction.

So I think that is just one example of how we can actually in the real world modify regimens for the appropriate patients.

**Dr. Callander:**
I think along those lines the CEPHEUS trial that you led, it's very impressive that you're using that fourth agent. You're using bortezomib, but actually for a limited amount of time and still showing a benefit from that, which I think was one of the best parts of that study design.

And I think patients often, particularly the older patients, can tolerate maybe 6 or 7 months of bortezomib, and then you get the advantage that you demonstrated, but you can sort of spare them some toxicity, I think.

**Dr. Usmani:**
Yes, and then talking about dose modifications, I think infection monitoring is also very important during that initial period. So, Dr. Callander, what is your typical strategy in managing patients, with those two things in mind?

**Dr. Callander:**
Yeah, I think a couple of things that I think are pretty much standard. You're using prophylaxis for VZV for varicella, and we do, if we're going to use dexamethasone, and that's one of the things that we try to be very proactive about in our older individuals, is getting the dexamethasone out as fast as possible. But if we are going to include some dexamethasone, we usually do have PJP prophylaxis built in.

And then I think it's just kind of patient awareness about if they are having symptoms, not feeling well, something more than just a sniffle, that they need to contact us and make sure that they're evaluated, particularly early on where a lot of these infections seem to happen, say in the first 6 months.

**Dr. Usmani:**
Yeah, I would agree with you. I think infections still remain the most important reason why patients end up in the hospital during that initial treatment, and it's so individualized. There are patients who might be presenting with a history of several months of recurrent infections where you have to kind of pay attention to even including antibacterial prophylaxis into their schema.

**Dr. Callander:**
So, Dr. Usmani, how do you choose between anti-CD38 antibodies for individual patients?

**Dr. Usmani:**
No, that's a very interesting predicament now because we have previously had one formulation that was IV and the other that was subcutaneous, and now we have both daratumumab and isatuximab with the ability to give them as subcutaneous.

I think there are certain practical considerations. The frequency with which we give these anti-CD38s is different amongst different regimens. We also have to pay attention to the particulars about the regimens and the pace with which patients would respond. We have to think about patient preferences.

And it's quite possible that depending on which geographic area or healthcare system patients are being treated with, there might be a preferential use of one anti-CD38 over the other, and insurances at the end of the day may also have that preference.

So I think it's so sometimes the main idea is an anti-CD38 antibody-based regimen is going to be very important for that initial care for the transplant-ineligible patients, whether it's a three-drug or a four-drug combination. And we have to figure out all those practical nuances.

**Dr. Callander:**
I think in the US in particular, what I've observed is prior to the reformulation of isatuximab, it was mostly combined with carfilzomib because the patient's coming in for an IV infusion, and that kind of made sense. My anticipation is with the OBI device that this is going to be probably accessed way more than it has been with these combinations, either a triplet or quadruplet.

Well, thank you, Dr. Usmani, and with that, our time is up. And we hope this quick case review has been helpful. Thanks so much for listening.

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