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

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Dr. Usmani:
Welcome. This is CE with GLC. I'm Dr. Saad Usmani, and I'm here with my colleague Dr. Callander.

Dr. Callander:
Thank you, Saad. I'm going to start with a case. This is a 72-year-old woman, but she's incredibly active. She walks 4 miles a day, and she came in with 4 months of increasing back pain. Her plain film showed a compression fracture of T12, and she turned out to be significantly anemic with a hemoglobin of 8, and her creatinine was also elevated at 1.44 mg/dL. Beta-2 was 4.7. Her kappa light chains were significantly elevated at 276 mg/dL. She was mildly hypercalcemic, and a bone marrow biopsy showed 70% plasma cells. She had a translocation of 11;14 and trisomies of 5 and 7. And then not surprisingly, her PET scan showed diffuse uptake in both the cervical and thoracic spine and also the intense compression fracture uptake.

So, for a patient like this, how would you decide whether that this particular patient is eligible to consider a transplant?

Dr. Usmani:
I think there are a few things that we have to kind of determine when we are thinking about patients in the newly diagnosed setting, and a big chunk of it is really dependent on the healthcare baggage or health condition baggage that they're bringing with them. It's performance status, their physiological age, what is their organ function, what are their other comorbidities. And really if they're fairly functional coming in with their diagnosis, then we lean more towards offering them a stem cell transplant.

And this paradigm may be shifting a little bit perhaps for the standard-risk patients, for high-risk patients in particular, I think transplant still has a role to play in it. So I guess part of the discussion that we can probably have is about whether disease biology has a role to play in our discussions with our patients and eventual recommendations.

Dr. Callander:
No, I think those are excellent points. I think autologous stem cell transplant still has offered I think many, many patients a chance to not only get a very deep remission but also to scale back on the amount of therapy that they need going ahead. And in particular with the studies that are going to show us that briefer maintenance is helpful, I think I still think that this is relevant for many patients. I don't know whether you are specifically not offering stem cell transplantation to people considered standard risk. In our program, we actually still are for some of the reasons I mentioned.

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Dr. Usmani:
Yeah, I think you're absolutely right. I think the goal of care, especially for standard-risk patients, has become how can we maximize their likelihood of getting into deep remissions, or what we call MRD negativity, and that is helping in figuring out whether we can deescalate in patients.

So for standard-risk patients who are starting induction therapy— and typically they're starting quadruplet induction therapy for patients —if they're getting to MRD negativity at a very deep level, say 10^{-6} after their initial induction, I think one can make the case for collecting their stem cells and then just moving them onto maintenance treatment. But if they haven't achieved that deeper response, then it's very reasonable to offer them. Today is the youngest they'll be, so their ability to tolerate that therapy would be much better.

And we have decades of data where we can actually offer them this option safely. It's like a short-term investment for long-term gains, I guess.

Dr. Callander:
Right, and I think you and I have been doing this for quite some time, and I think you, I'm sure have like I do, patients who are post-transplant who continue to do extremely well for a number of years. And I sort of think of myeloma treatment sometimes as maybe a chess game, that you have to have a certain amount of moves that you're going to make. And I think right now particularly with some of the data looking at quadruplets followed by stem cell transplant, you have this big block of time where people are going to be pretty healthy and pretty well and be able to be around for maybe the next big innovation.

But I do agree with you. There are some patients who I think are opting for stem cell storage, particularly if they are MRD negative after induction.

Dr. Usmani:
So, Dr. Callander, why are we moving away from VRD to quadruplet induction regimens in newly diagnosed transplant eligible patients?

Dr. Callander:
Well, I think that there's now ample data that some of the goals we want to achieve, being great control, MRD negativity, while still trying to minimize any excessive toxicity, anti-CD38 antibodies certainly have been proven in large phase 3 randomized studies to offer benefit here.

And I think it's just what we were talking about earlier, you want to offer the patients up front the best shot, the best induction regimen you can come up with, and I think most patients, I think you would agree, who are transplant eligible are going to tolerate a quadruplet regimen just fine.

I do think this is the reason why quadruplet regimens are now listed under the NCCN Guidelines as preferred regimens, with sort of the top recommendation for use. And I'm sure that's what you're offering all of your patients as well.

Dr. Usmani:
Absolutely. I think we've all moved towards the quadruplet induction for patients away from the triplets, and amongst the therapies we have, honestly, the anti-CD38 antibodies are probably the easiest to administer without– in terms of adding any additional side effects to the patient's profile.

In fact, amongst the treatments we have, while we're treating patients with induction treatment, you don't dose adjust for the anti-CD38; you have to do it for the proteasome inhibitor. You have to do it for the immunomodulatory drug and steroids, of course, but typically not for anti-CD38s.

And I think across the board, not just in the United States but in Europe and other countries as well, quadruplets with anti-CD38s are becoming frontline treatment.

Dr. Callander:
And what are your thoughts about— well, we actually had a recent announcement about the development of isatuximab given with an

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on-body infusion device, an OBI device, but had you previously picked between subcutaneous or intravenous administration?

Dr. Usmani:
Not really. I mean, we know that we've had the subcutaneous formulation of daratumumab, which came in fortuitously around the time when the pandemic was hitting back in 2020, and honestly, it was a game changer in terms of patient convenience and being able to give them less chair time while delivering effective therapy. So we've been proponents of the sub-Q formulation of anti-CD38s.

And it's good that we actually have isatuximab coming in with that formulation now, with an on-body device, which will help deliver that therapy in a shorter period of time. So again, the more options for us, the better.

Again, if we go with a broader 30,000-foot view, there are many parts of the world that do not have anti-CD38s available, and having a healthy competition with different products in the market helps in getting more access to our patients.

So I think it's a welcome addition to the armamentarium we have, and it will ease the administration for many of our patients.

Dr. Callander:
So, I think one thing that has been seen in the studies that include anti-CD38 antibodies is a mild increase perhaps in some respiratory infections. I think that's been my experience, as opposed to the triplets without. What's your approach to managing infection prophylaxis in these patients, and do you ever use IVIG?

Dr. Usmani:
Yeah, so we watch patients very carefully for their immunoglobulin levels on a monthly basis while they're getting myeloma labs. In general, for newly diagnosed multiple myeloma patients, I think due to the initial disease burden and the qualitative and quantitative immune deficiency, they would be at risk for infections. But if disease is getting under better control and they're still remaining hypogammaglobulinemic, I think providing them prophylaxis with IVIG is reasonable.

Many of these patients, we already have them on VZV prophylaxis. Sometimes we would even consider PJP prophylaxis based on their prior infection history. But I think it's a very important part of supportive care considerations during their treatment.

Dr. Callander:
Yeah. No, I would agree with that. I mean, we have all of our patients on varicella prophylaxis, and we actually follow kind of the TEAMMs trial model that will offer a quinolone the first few months of induction because we actually have seen some early pretty serious infections with patients. Not so much I think reflecting the toxicity of the treatment, but more the underlying immunosuppression that they're walking in the door with because of their myeloma activity.

Dr. Usmani:
Well, with that, our time is up. We hope this quick case review is helpful. Thanks so much for listening.

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