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Choosing and Sequencing Regimens in Relapsed Multiple Myeloma

Announcer:
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Dr. Mikhael:
Hello, my name is Dr. Joseph Mikhael, and I want to chat with you today about Choosing and Sequencing Regimens in Relapsed Multiple Myeloma.

This may be one of the most challenging aspects of relapsed multiple myeloma. Now that actually we have so many choices, when do we use one regimen over to other? And how do we sequence them? And I don't think there's a perfect answer to these kinds of questions. But I'll share with you my approach and how I think about relapse myeloma.

First of all, there really is no perfect sequence, right? There's no absolute algorithm. We don't just say, 'I do this first and this second and this third,' we really go based on a series of principles when a patient has either early relapse or later relapse disease even out to triple class-refractory. Some of those principles include seeking the deepest response possible. Differentiating high-risk versus standard-risk myeloma, balancing the efficacy and toxicity of some of these regimens, and introducing new mechanisms of action so that we can overcome drug resistance.

Well, pragmatically, what does this look like in the clinic? Well, we typically divide patients into LEN-refractory and LEN-sensitive, knowing that most patients are LEN-refractory, having had lenalidomide in the maintenance setting after transplant or in the frontline continuous setting in patients who didn't go to transplant. If we go and look to the NCCN guidelines, it really almost becomes just a laundry list of choice as opposed to a very directed approach, whether it's an earlier relapse or in later relapse disease.

So let me just quickly share with you what do I do? What does Dr. Joe do? Well, when someone has their first relapse, or they're in their second line of therapy, it depends of course on what they've had before. If they've had a VRd or DVRd regimen followed by a transplant and maintenance lenalidomide, I tend to favor a DPd or an isa/Pd regimen, when they are standard risk or they haven't been on lenalidomide for a long time. By contrast, if they have high-risk disease, or have had a short term on lenalidomide, I'll favor a carfilzomib approach like DKd or isa/Kd. If a patient has just been on DRd, like the MAIA regimen, and not had a transplant, staying on DR and are now relapsing, well, I don't want to give them a daratumumab or isatuximab regimen because they're resistant immediately to a CD38 I'll typically give them KPd, or in certain higher-risk settings like p53 deletion, I would consider selinexor or carfilzomib/dex. Depending on the jurisdiction you're in. You may also in these situations, consider PVd, or pomalidomide/bortezomib/dexamethasone. And don't forget there are some patients who can benefit from a second transplant if they had a long remission from the first.

Well, what about third-line therapy? Well, if they had had pomalidomide as in the previous discussion, then I will go now to a carfilzomib-based regimen, either with selinexor or carfilzomib. If they had had the carfilzomib side, now I'll go to a pomalidomide regimen, either with selinexor, or typically with elotuzumab and maybe even cyclophosphamide. And if patients had both carfilzomib and pomalidomide, then I would typically go towards a selinexor-based regimen, typically with daratumumab, bortezomib, or even with dexamethasone alone.

And then lastly, when we come to fourth-line therapy, so their third relapse, this is actually often the most challenging space, because we know when we get to fifth-line therapy, patients can now be eligible for CAR T-cell therapies and bispecifics, but they must have had 4 prior lines. So often this fourth line becomes really a challenging spot. So I will try to look back and see are there things that they have not seen yet that they haven't been exposed to. Always consider a clinical trial if it's available. And don't forget alkylating agents. I think very often, we now, with fewer patients going to transplant, patients haven't seen much alkylate, or whether we use it as melphalan or cyclophosphamide, that that can be used in conjunction with other agents that they may have.

So hopefully, this strategy of thinking will help you as we walk through the multiple lines of therapy. Now of course, as we discussed in other contexts, some of those later line treatments like CAR T-cell therapy, and bispecifics are likely going to arrive into earlier stage myeloma in the near future. But in the interim, we want to optimize the regimens we have and sequence them in the best way that we can.

Thank you very much for your attention.

Announcer:
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