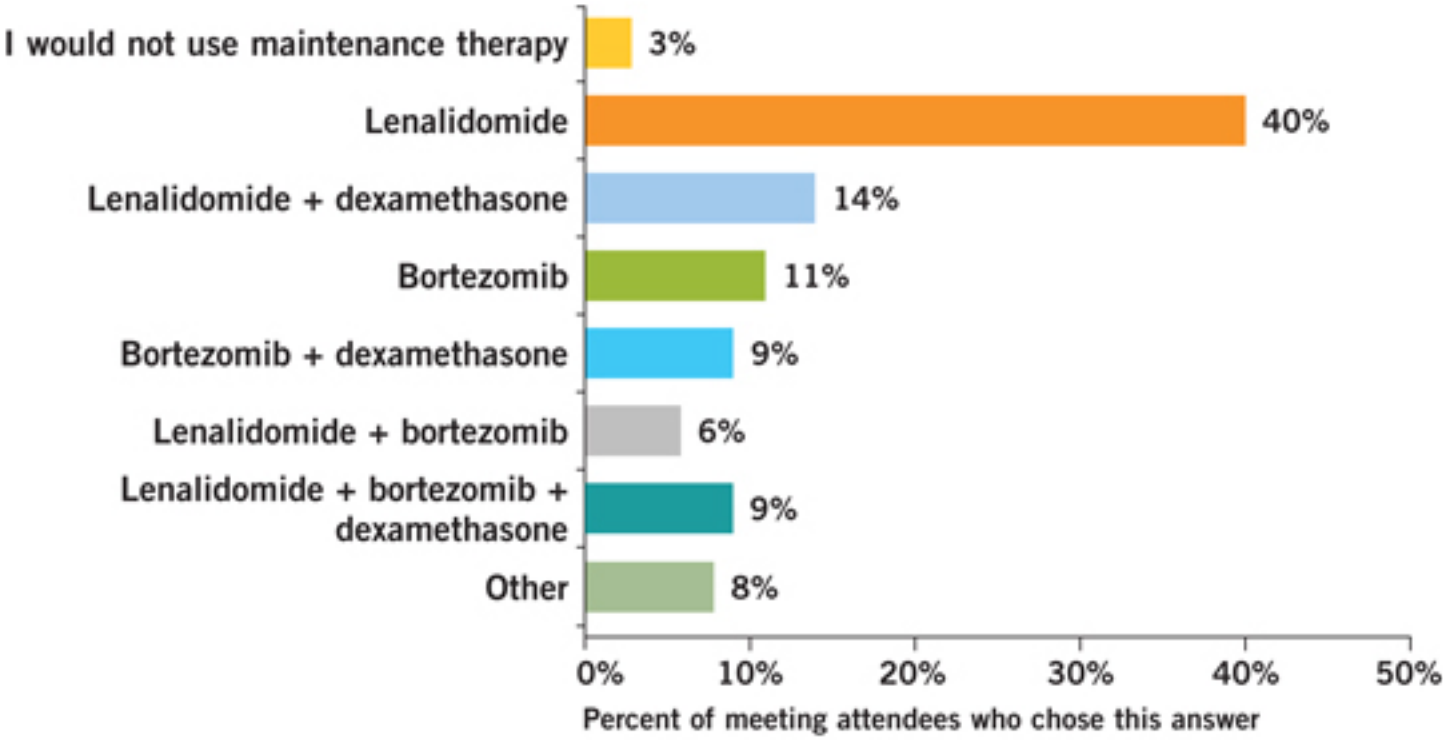
Year in Review

Proceedings from a Multitumor CME Symposium Focused on the Application of Emerging Research Information to the Care of Patients with Common Cancers

Novel Agents: Ixazomib, Oprozomib, Panobinostat, Elotuzumab and Daratumumab — Sagar Lonial, MD

A 60-year-old patient with ISS Stage II, high-risk (del17p) MM receives induction RVD, undergoes ASCT and achieves a very good partial response. Whether or not you administer consolidation therapy, what would be your choice of post-transplant maintenance therapy?



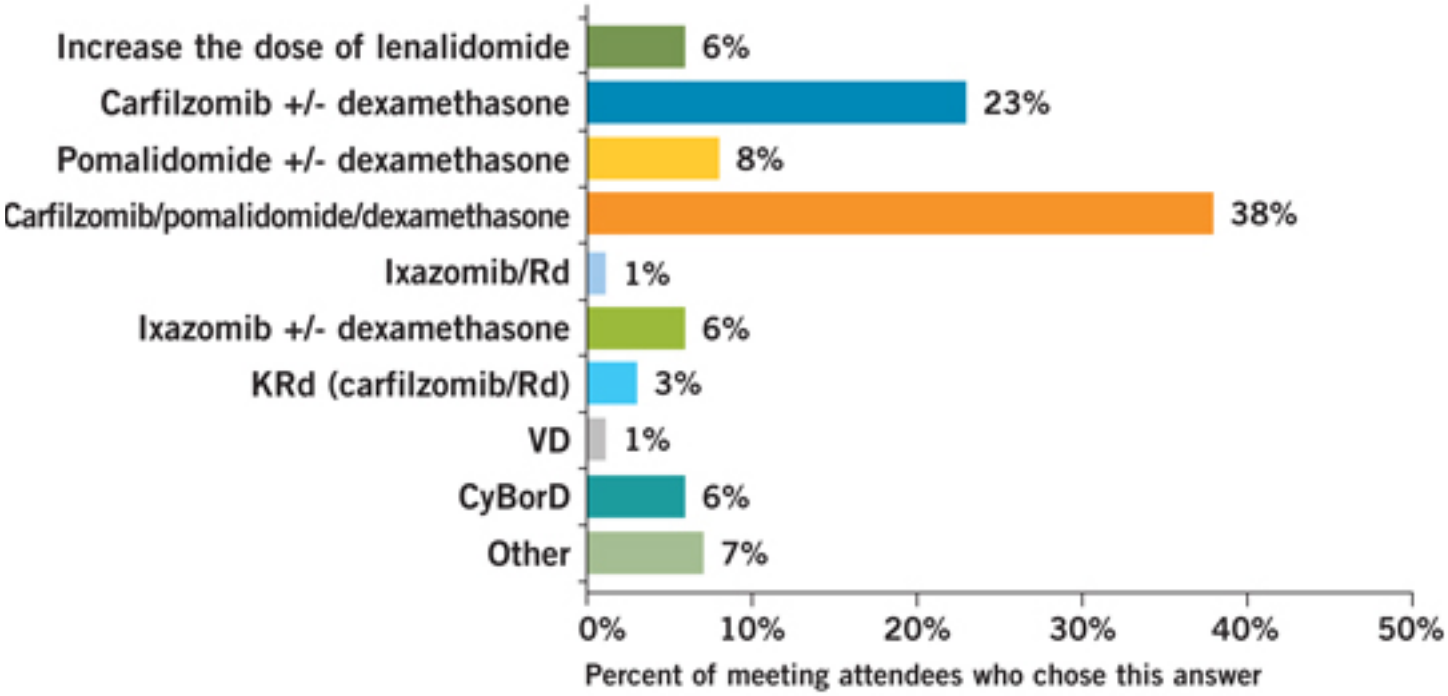
DR LOVE: Sagar, we wanted to get very, very practical and pragmatic, so we picked a situation of a 60-year-old patient with high-risk disease, so (del)17p, gets RVD/transplant, has a good partial response. And we asked the audience: Regardless of whether or not any kind of consolidation, would you use post-transplant maintenance and, if so, what kind? Looks like the vast majority of people would use, but the most common answer is lenalidomide. What would you do yourself, Sagar, in this situation?

DR LONIAL: I think as we try and talk about personalized medicine or precision medicine and all these new buzzwords in oncology, to me, treating all patients in the maintenance setting in the same way doesn't make a bit of sense. This is somebody, based on our own data, I would say, who should get triplet-based consolidation with RVD for 3 years, which is what we've done.

I know it sounds tough to do. My middle name is not Barlogie, but what I will say is that, for high-risk myeloma, the consequence of letting the myeloma come back is a lot worse than the idea of 3 years of intensive maintenance therapy.

Because once it comes back, especially in the context of 17p deletion, genomically and genetically it's a much more complicated disease to treat. I'd rather work on suppressing it for a longer period up front than letting it come back and then having to deal with it.

What is your usual treatment recommendation for a younger patient with MM who receives RVD followed by transplant and experiences symptomatic disease relapse while completing the second year of maintenance lenalidomide?



DR LOVE: One of the things that we're talking about today is the art of oncology. And sometimes there are multiple evidence-based options that you can defend. Relapsed/refractory myeloma certainly fits that category, so, Vincent, we presented this scenario. We said: How do you usually approach a younger patient, gets RVD and transplant, then has symptomatic relapse during the second year of maintenance lenalidomide?

You would expect a lot of people are relapsing on maintenance lenalidomide because it's being given so often and it's being given indefinitely. What we see here is actually a split, again, some people thinking about a triplet, so carfilzomib/pom/dex, for example, and a few people a single agent. Vincent, how do you think this one through?

DR RAJKUMAR: For this particular patient I had a choice that was quite different from what the audience have answered. I think we heard that most of us are thinking, "For a young patient, relatively fit, first relapse, let's use a triplet." If you're going to use a triplet, which one to use? If you look here, the patient's had RVD and transplant but is failing on lenalidomide maintenance.

Generally, we at Mayo would probably use CyBorD first line, simply because it's extremely well tolerated and very convenient for the patient. They can go for a couple of years, or a year or two, with that regimen, and then use the ones that are more cumbersome, like carfilzomib-based regimens. But I cannot quarrel because I don't have Phase III data. You're talking about multiple active triplets. How do you pick among them?

DR LOVE: But there is a difference in terms of triplet versus doublet. You refer to the fact that there was disease progression on an IMiD. Where do things stand in terms of cereblon as a marker to make decisions like this? Keith Stewart has been doing work, along with others. Is that getting anywhere near prime time?

DR RAJKUMAR: Well, they're building something like a CLIA-certified test that you can use. But I don't think that I would use cereblon by itself to decide when to use lenalidomide or when not to. I think the data are all based on very small numbers of patients. These drugs work in combination even when the single agent doesn't work. Car/pom/dex, for example, might work even in a patient with IMiD-refractory disease.

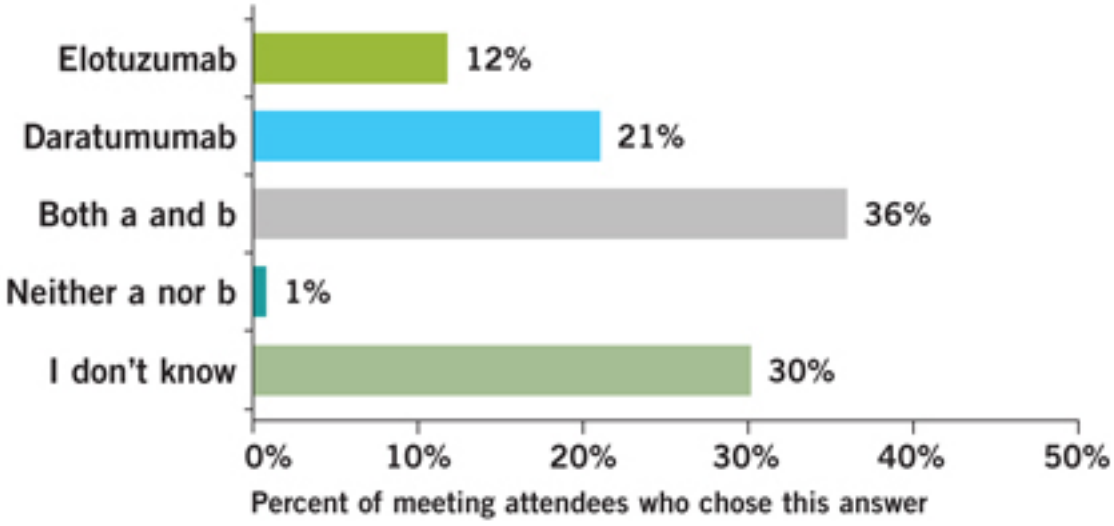
DR LONIAL: Neil, can I make a comment about this case real quick? If you're thinking about the art of medicine, as you mentioned, this is a patient that relapsed on len maintenance within 2 years of their transplant. We know that patients who relapse within 1 year of their transplant, who get no maintenance, represent a very high-risk category of patients. Even if their genetics and everything else is okay, relapsing within a year of an autograft is certainly a poor prognostic feature.

I would argue relapsing within 2 years on len maintenance is also, to me, a high-risk subset of patients because the unmaintained duration of remission should be 2 years. If they're relapsing within 2 years on maintenance, that makes me a little concerned. This might be somebody, for that reason, that I would know which preferential triplet to go with, using something like car/pom, because we know car/pom is very active in a high-risk cohort of patients.

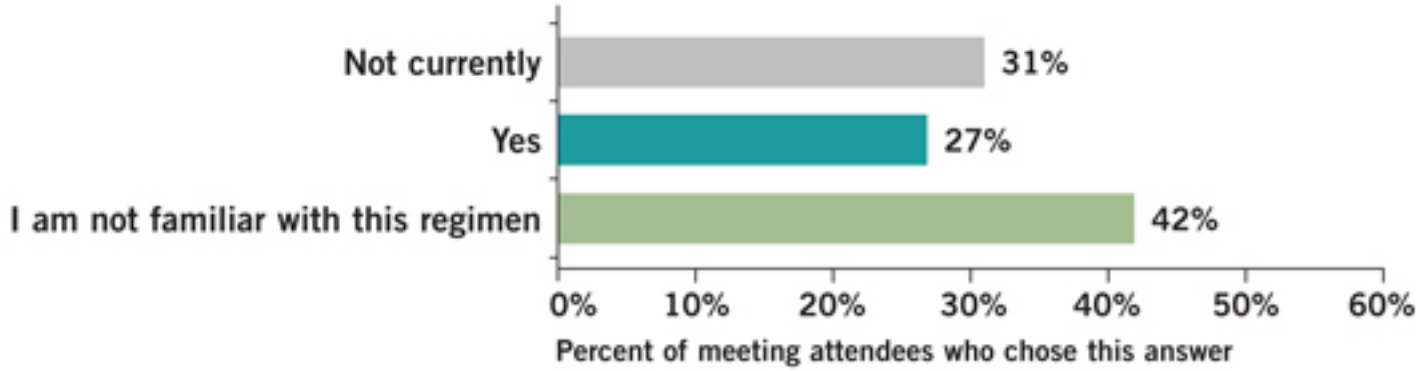
DR LOVE: Is there a role, though, for carfilzomib by itself, without dex, or pom without dex, Sagar? And what kinds of patients would you do that in — older, frail?

DR LONIAL: I think when patients have had a second autotransplant, because they've had such great response to the first, we may use single-agent pom in the maintenance setting in that situation. There isn't a lot of data for either of those as single agents. Remember, the dex that goes with carfilzomib is usually pretty low. All you really need is 4 mg on each dosing day of carfilzomib for the first cycle. Then we will often, for patients who are steroid sensitive, get rid of that as well. Carfilzomib can be used beyond cycle 1 without corticosteroids.

Which of the following monoclonal antibodies has shown significant single-agent activity in patients with relapsed/refractory MM?



Do you see a role for the combination of panobinostat/carfilzomib in your practice?



DR LOVE: On that list of 25 was another myeloma drug that was approved earlier this year, panobinostat. It was approved with bortezomib. Just talking to investigators and trying to figure it out, I was kind of confused about what it really meant. It's always tricky when you combine things. So first of all, I see most of the audience hasn't heard about this, which is not surprising. It was not a major paper. Can you explain what you're thinking about this? Is this something that really offers a significant benefit to patients?

DR LONIAL: One of the challenges of trying to understand how to use the PANORAMA 1 trial in clinical practice is that it did a lot of things that we don't do regularly anymore. First of all, it gave IV bortezomib, which we don't do. The modifications of doses and schedules were probably 4 or 5 years old in terms of trying to keep patients on schedule. The overlapping toxicity of GI issues, nausea, vomiting and diarrhea, between an HDAC and a proteasome inhibitor, particularly bortezomib, were such that I think it ultimately limited the efficacy of that trial.

What carfilzomib plus panobinostat allows you to do is change the schedule of panobinostat and give it with a proteasome inhibitor like carfilzomib, where the GI toxicity is almost nonexistent. When you do those two things together, I think you get pretty significant and sometimes durable responses.

DR LOVE: Are you doing that right now in your practice?

DR LONIAL: Yes.

DR LOVE: Carfilzomib with panobinostat?

DR LOVE: Vincent?

DR RAJKUMAR: I have had a few patients that I have put on carfilzomib plus panobinostat as well.

DR LOVE: Interesting. It's indicated for bortezomib, correct?

DR RAJKUMAR: Correct.

DR LOVE: But I guess same class of drugs.

DR LONIAL: There are three trials looking at car/pan together. It's not like there's one small Phase II. There's now at least 100-plus patients that you have data on.