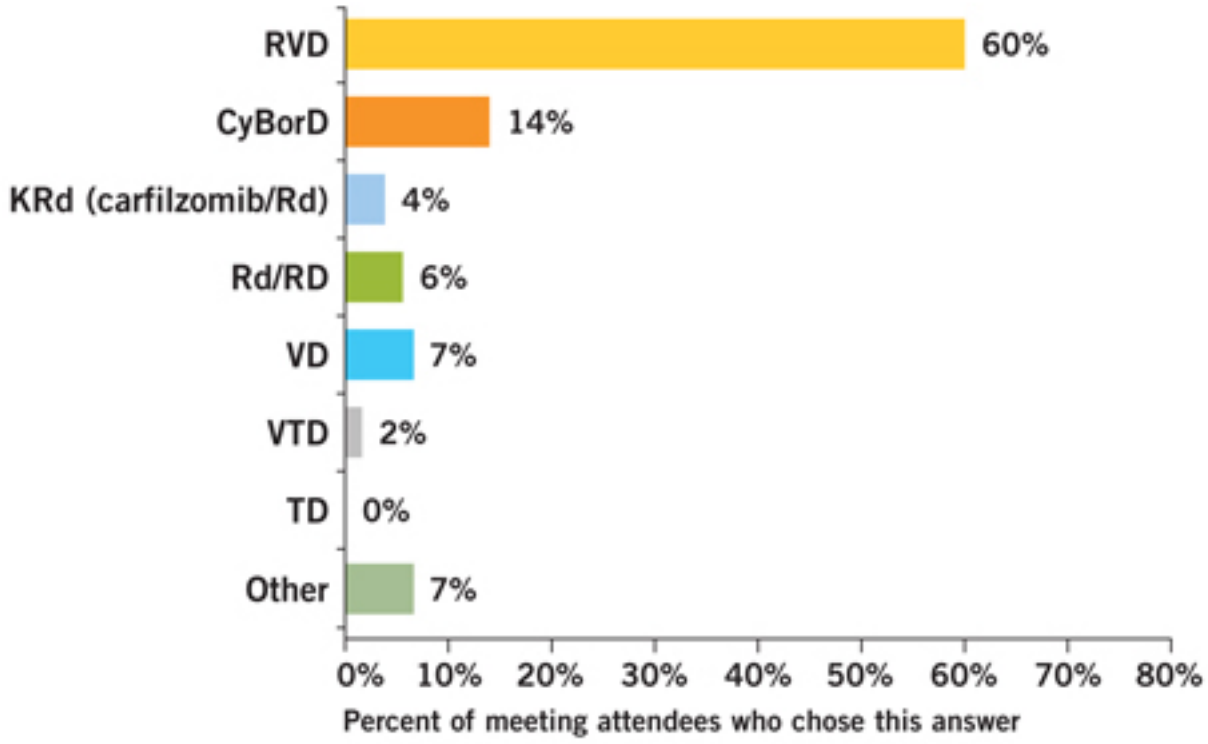
Year in Review

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

Induction, Consolidation and Maintenance; Doublet versus Triplet Combinations in Relapsed/Refractory Disease — S Vincent Rajkumar, MD

An otherwise healthy 60-year-old patient presents with ISS Stage II multiple myeloma (MM). Cytogenetics and FISH reveal no high-risk features. In general, which induction treatment would you most likely recommend?



DR LOVE: Vincent, this is certainly a trend that we've been seeing in the last few years when we ask a pretty straightforward question about the initial approach in terms of induction therapy to a younger patient without any high-risk features. We're seeing more and more answers of triple therapy. You see just about everybody here says either RVD or CyBorD. There are people, particularly a lot of your colleagues in the Mayo Clinic, who've talked about maybe just a single agent with dexamethasone — for example, Rd. How are you thinking this one through today, Vincent?

DR RAJKUMAR: Right now, we are awaiting results of the big SWOG trial, which compared Rd versus VRd. Those results should be available in December. But I think I would agree with the vast majority of the audience that, knowing some of the results ahead of time, I have changed my mind. And RVD is probably going to be my front-line standard for newly diagnosed myeloma patients and particularly the standard- and the intermediate-risk groups.

DR LOVE: We had your colleague Shaji Kumar here in Chicago last week. I was surprised because I hadn't heard this from you all. Is this kind of a change in the way you think it through, and why?

DR RAJKUMAR: We've always been data driven. There were two small Phase IIs, and this is the most expensive regimen on the planet with $200,000 per year. If I'm going to recommend a $200,000 regimen, I cannot do it based on two small Phase IIs. We were waiting on the Phase III. The Phase III is finally here. Nobody has seen the results. Some of us have had a preview. I don't want to come here 2 weeks before the results come out and say that Rd is standard when I know it's going to change in 2 weeks.

DR LOVE: Interesting. Which study are you talking about?

DR RAJKUMAR: I'm referring to the United States SWOG trial that compared Rd versus VRd. It's up front, newly diagnosed. The first Phase III.

DR LOVE: Sagar, I didn't know if I was hallucinating last week or not. I saw the actual transformation, but now I understand why. He didn't explain that. That's very interesting.

DR RAJKUMAR: There's also one other trial, Neil, of RVD/transplant/maintenance or RVD alone and maintenance. That trial shows that both arms have a survival rate of about 88% at 4 years, which is unprecedented for newly diagnosed myeloma. These two trials, Phase IIIs, put together, give us the best data on RVD we have right now.

DR LOVE: Wow! So basically up-front transplant versus delayed is about to report? You're talking about the IFM Dana-Farber transplant now or not?

DR RAJKUMAR: Yes.

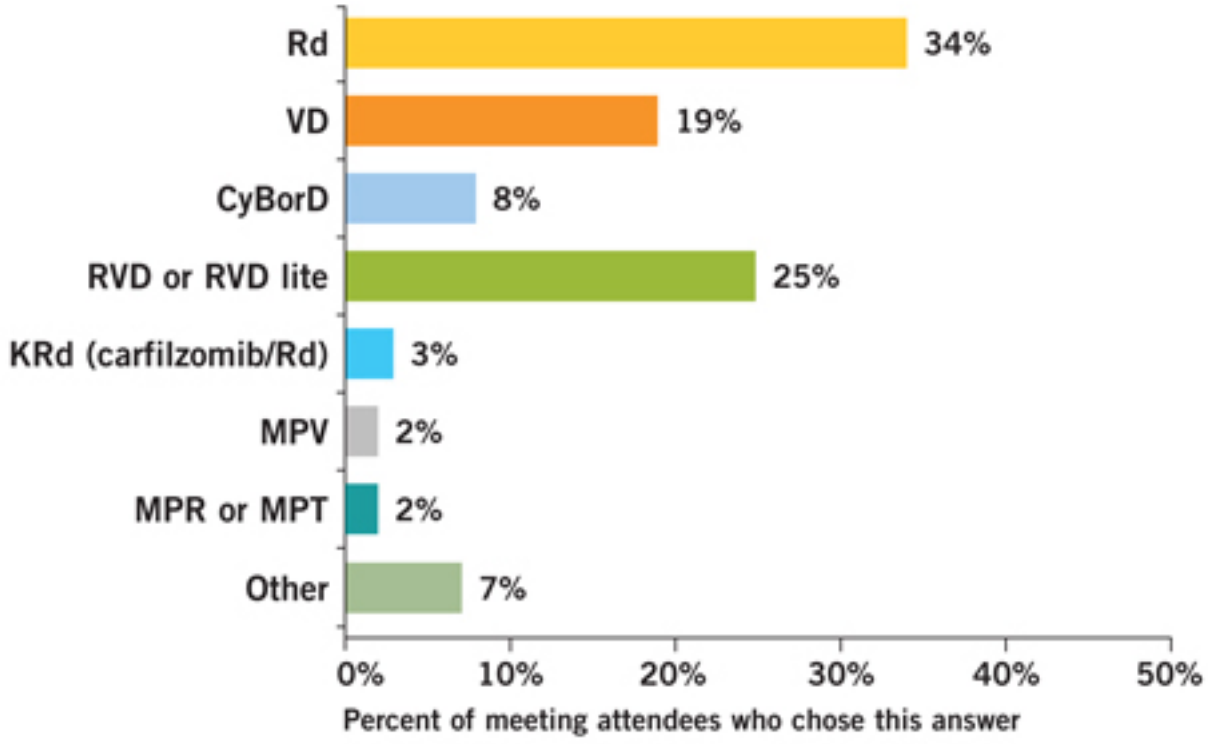
DR LOVE: So you're saying that's going to show that they're the same? Or you don't need transplant?

DR RAJKUMAR: All I can say is the results that were presented at the Rome meeting show that the survival is identical, whichever way you do it. They have a progression-free survival difference, which they will present at ASH.

DR LOVE: Wow! We've been hearing from investigators, Sagar, very pro-transplant up until today. Is that going to change?

DR LONIAL: I don't think so. I think that what Vincent's referring to was just that the survival difference between the two arms is not there. But the follow-up is still relatively short to see a survival difference. I think what we know from Dr Rosell's publication in *JCO*, which was 3 of RVD, single transplant, consolidation and maintenance therapy, the overall survival is huge for that small pilot study. And I think it's going to be mimicked in the larger Phase III trial as well. I don't think transplant's going away.

What is your usual induction regimen for a 75-year-old otherwise healthy, transplant-ineligible patient with ISS Stage II MM and no high-risk features?



DR LOVE: We asked this audience about older patients, and it looks like there's a little bit of a split — Rd, RVD or RVD lite or bortezomib/D with or without cyclophosphamide, so kind of split up a little bit. How do you think this one through, Sagar?

DR LONIAL: For me, this one is really about frailty. To me, that's really how you make the judgment about a doublet or a triplet. If a patient is truly a frail patient, like in Ruben Niesvizky's up-front trial that was published in *JCO* a few months ago, where he compared bortezomib/dex versus bortezomib/thalidomide/dex versus bortezomib/melphalan and prednisone, what was clear was that for older, frail patients, a doublet probably is as good as a triplet. If this were a relatively fit but still transplant ineligible 75-year-old, I would try and use a modified RVD to treat them. But if they're truly frail, then I think getting a triplet into them is a real challenge.

DR LOVE: Vincent, looking back at our first two regional meetings, Dr Fonseca, your colleague, said Rd. Dr Kumar said Rd. What do you say?

DR RAJKUMAR: I think I would agree with Sagar. It really depends on frailty. If this was a 75-year-old frail patient, definitely Rd. It's one of the easiest regimens to take. Patients can go many years, probably 3 years or longer, without needing a change in therapy. So that's a very reasonable option to use. But if the patient's more fit, the more fit they look, I would move more and more toward RVD and RVD lite. I'm becoming like Sagar a little bit, which is scary.

DR LONIAL: We're just glad you've given up the horse and buggy and are moving to the combustible engine.

DR LOVE: Any thoughts, Sagar, about dosing in older patients — 75, 80, 85 years old — both in terms of the, quote, RVD lite approach as well as just Rd?

DR LONIAL: To me, there are a couple of things that you really want to try and think about adjusting in terms of dose. The first is the corticosteroids. If you're above the age of 70, giving 40 mg even once a week may be a challenging thing to do. And, again, in the frail patient, it's not about how quickly you get a response, but it's how good your response can be over the course of a longer period of time.

I had a patient come to me that was started on full-dose Rd at the age of 85. And guess what? She melted, fell apart. The first thing I did was switch to a little bit of prednisone, rather than dexamethasone, and she's done fine. That's the first. The second is, really look at creatinine clearance when you think about dosing the lenalidomide. It's easy to do now. Our computers are doing creatinine clearance for us, and that helps. And then bortezomib, going to weekly instead of twice weekly is an option. I still use twice weekly when I do RVD. But for older patients, going to the once-a-week, I think, is a little easier.