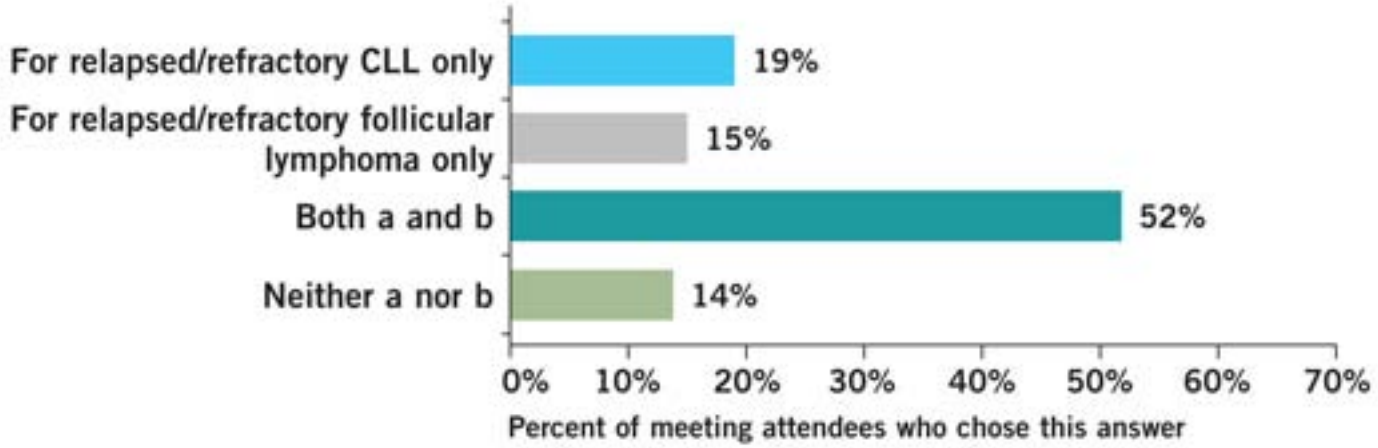
Year in Review

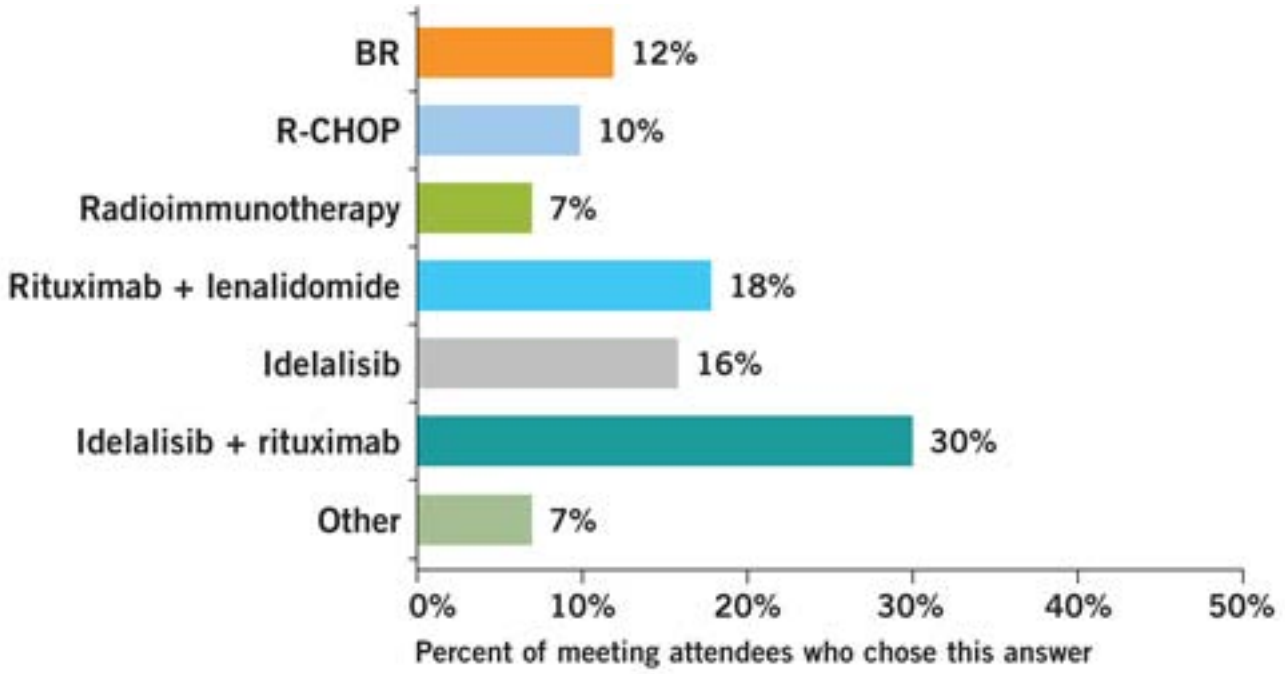
Proceedings from a Multitumor CME Symposium Focused on the Application of Emerging Research Information to the Care of Patients with Common Cancers

Follicular, Indolent and Mantle-Cell Non-Hodgkin Lymphomas — Brad S Kahl, MD

How do you currently use idelalisib in your practice?



A 76-year-old otherwise healthy patient with follicular lymphoma receives BR followed by 2 years of rituximab maintenance but 2 years later develops disease progression. Which treatment would you most likely recommend at this point?



DR LOVE: We want to begin talking about an FL situation that's pretty common, a 76-year-old patient, otherwise healthy, with follicular lymphoma, Brad, who gets probably the most common therapy for a patient like this, BR, 2 years of rituximab, then 2 years later had disease progression. The most common answer of the audience is idelalisib-R, although, interestingly, some people talk about idelalisib by itself. Brad, how do you think through this situation?

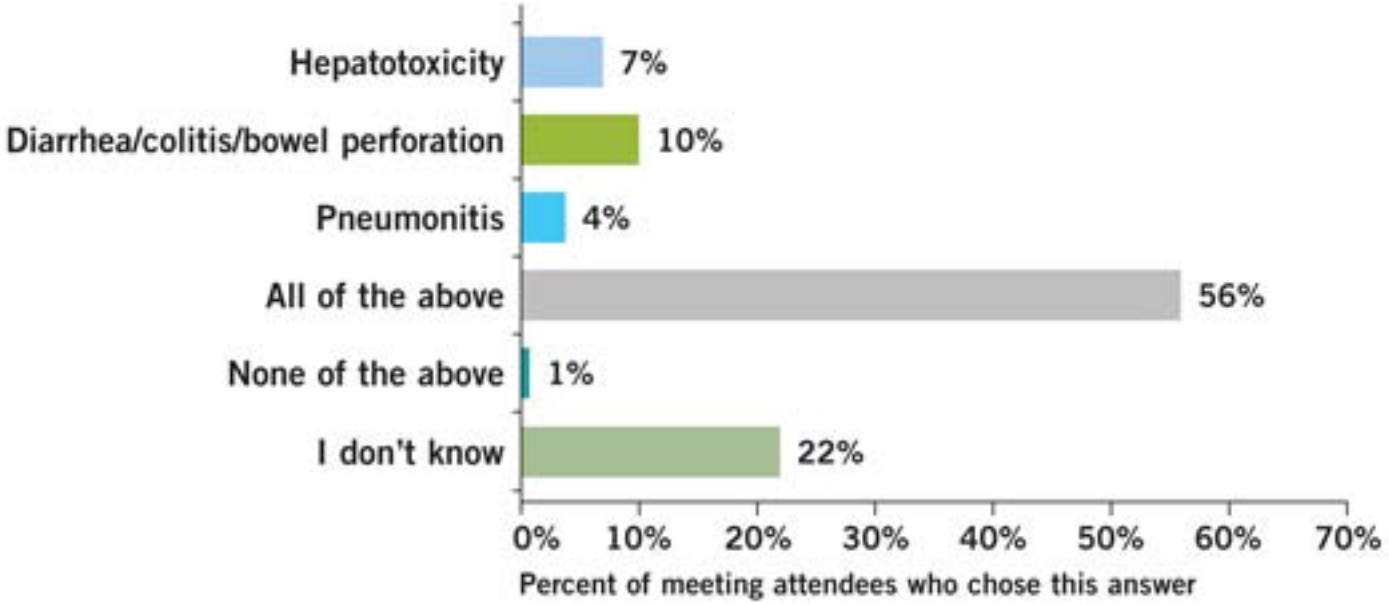
DR KAHL: Well, the patient's 76, so getting older. That limits your options to a degree. This is not the kind of patient we would be thinking about stem cell transplantation. There are a variety of reasonable options here and, hence, you see the spread there. Certainly, a 76-year-old can handle R-CHOP. But the response to traditional cytotoxic therapy, meaning BR, wasn't that great in this patient.

Intellectually, it's more attractive to get away from cytotoxics and try something with a fundamentally different mechanism, something like the idelalisib/rituximab combination or the rituximab/lenalidomide combination. Mind you, lenalidomide is not approved for follicular lymphoma, but sometimes you can get it off label. Those sorts of combinations would be more attractive to most investigators in a patient like this.

DR LOVE: Craig, a few people here talked about radioimmunotherapy. What do you see as the role right now for radioimmunotherapy in FL, and what about in this situation?

DR MOSKOWITZ: Shockingly, I gave my first dose of Zevalin in the last 6 years this week. That was a patient who had Grade 3A follicular lymphoma, who had a PR with a residual 7-cm perirenal mass. I thought it was reasonable to give him radioimmunotherapy, but the era of radioimmunotherapy, I would say, has ended. I'm confused at who even owns the radioimmunotherapy drugs half the time and who to call. Outside of giving Zevalin with a transplant-conditioning regimen, I think it's pretty much done.

Which of the following serious side effects is associated with idelalisib?



DR LOVE: Mike, it would seem that some kind of a relapse situation like this might be where you think about idelalisib. That's one of the drugs, more than two dozen, that have been approved in the last couple of years. We asked about the issue of tolerability. Most of this audience is aware that hepatotoxicity, diarrhea and colitis and pneumonitis have all been seen. Can you comment, Mike, on your own experience with the tolerability with idelalisib and specifically these 3 problems?

DR WILLIAMS: The hepatotoxicity is often a transaminitis. That's something that you can work around at times, depending on the severity. The diarrhea comes in two forms. Sometimes it's a little hard to tease out because you can have diarrhea as a side effect, but the severe inflammatory colitis tends to come on more at 8 or 9 months. The pneumonitis is often several months into treatment. I have seen pneumonitis, but fortunately have not had significant problems with the other toxicities.

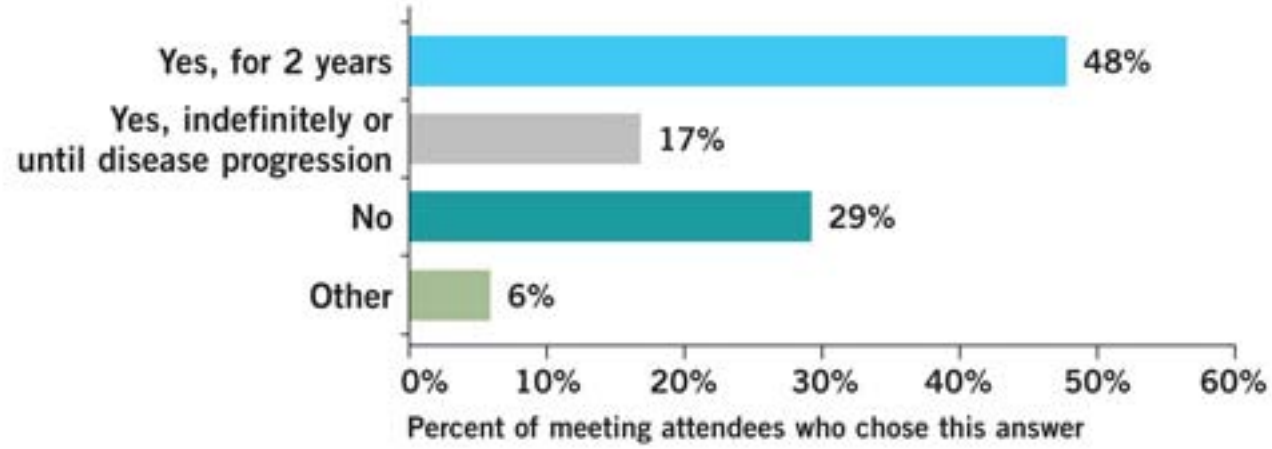
DR LOVE: Can you talk a little bit, with this delayed inflammatory type of colitis, how you approach it clinically, Mike?

DR WILLIAMS: What we've generally done is, of course, stop the drug and institute relatively high-dose steroids.

DR LOVE: But most of these people get diagnosed or they've been doing well for a while. They go into an ER for a diarrhea kind of thing?

DR WILLIAMS: At least within our population of patients, they're being followed pretty closely by us. They may end up with an acute problem, but generally we are aware that this is brewing. The patients are well-informed to be alert to some of these side effects.

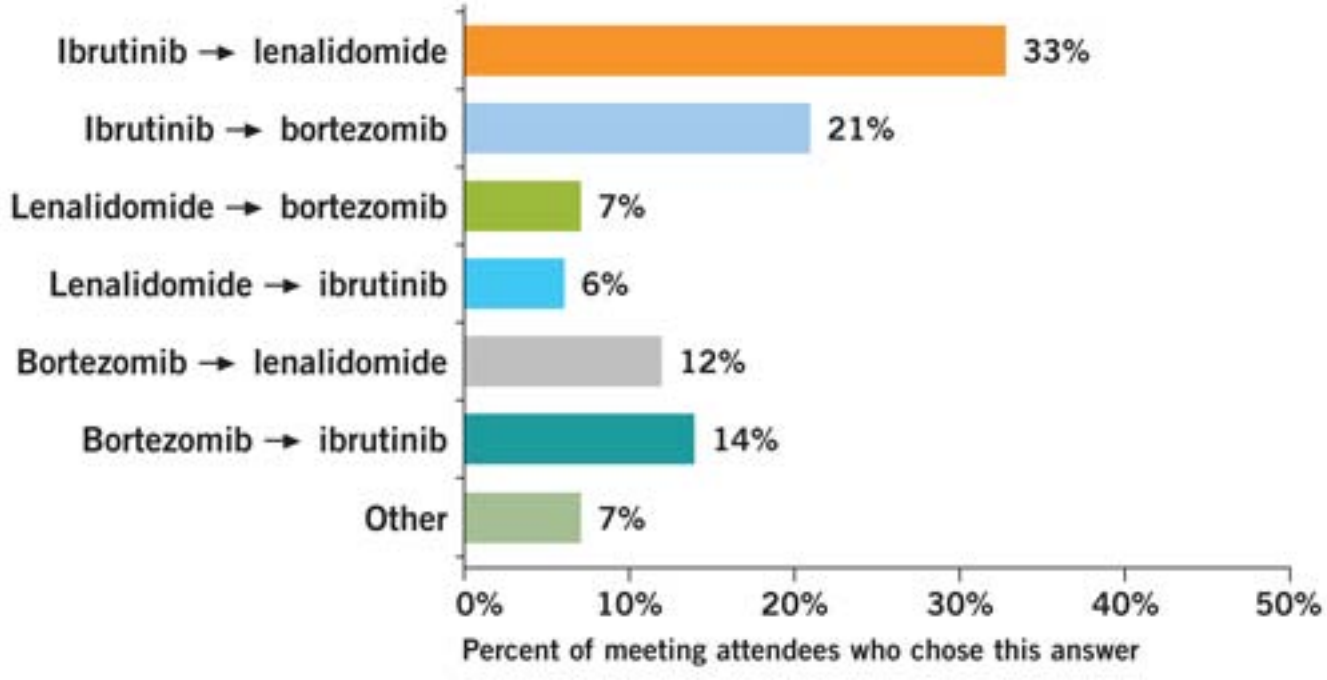
In general, do you recommend maintenance rituximab for younger patients with mantle-cell lymphoma (MCL) who have received rituximab/chemotherapy followed by transplant?



DR LOVE: We did see some data this year — maybe not as exciting as some of the new agents but still potentially practice changing from the last ASH meeting — looking at maintenance R in the younger patient who gets transplant. And it looks like that message has gotten through to the vast majority of the audience.

DR FANALE: I think if you are going to use a transplant-based strategy, which is a little bit different than, I think, what we do personally at Anderson, but if you're going to be taking these patients through R-DHAP and then doing a consolidative autologous stem cell transplant, there is clear data now that shows improved progression-free survival for the patients who get maintenance rituximab versus those who do not.

A 75-year-old patient with MCL responds to BR but after 18 months develops moderately symptomatic disease progression. The patient is not a candidate for transplant. In general, what would be your next 2 systemic treatments for this patient?



DR LOVE: Brad, wanted to get the audience's take on their general algorithm to relapsed disease, so we talk about an older patient, 75 years old, with mantle cell, gets BR, but then has moderately symptomatic disease progression. We wanted to know — there are obviously 3 approved strategies out there right now, ibrutinib, lenalidomide and bortezomib — how people sequence these. It looks like a little bit all over the chart. Can you talk, Brad, about how you think through which drug to use when?

DR KAHL: Sure. If you just think in terms of response rates, ibrutinib, of those choices, has the highest response rate. It should be around 60% to 70% in relapsed mantle-cell lymphoma. So I would go with ibrutinib first. It's generally a well-tolerated medication, very favorable safety and side-effect profile. We've talked about the bleeding and the a-fib and things like that. The responses in mantle-cell are not as durable as they are in CLL, so people should be aware of that.

I would say the second choice would be lenalidomide, based on the response rate. I would always give lenalidomide with rituximab in this setting. The response rate is substantially higher when you combine lenalidomide with rituximab compared to lenalidomide alone. Bortezomib would be the third choice with a response rate of around 3%. There is the issue of peripheral neuropathy to be wary of.

DR LOVE: Mike, what's your clinical experience with these approaches? And we know in the myeloma world, where you've got the oral proteasome inhibitors like ixazomib coming along — are they being looked at in mantle-cell?

DR WILLIAMS: They are. Studies with the oral drugs are under way now. In terms of my approach, I agree with what Brad said. The caveat you mentioned with bortezomib is neuropathy, but generally weekly subQ is pretty well tolerated. The problem I've had with lenalidomide in patients such as this is that their counts often are a bit difficult to manage. They get a fair amount of cytopenia. So you have to be aware of the balanced toxicities.