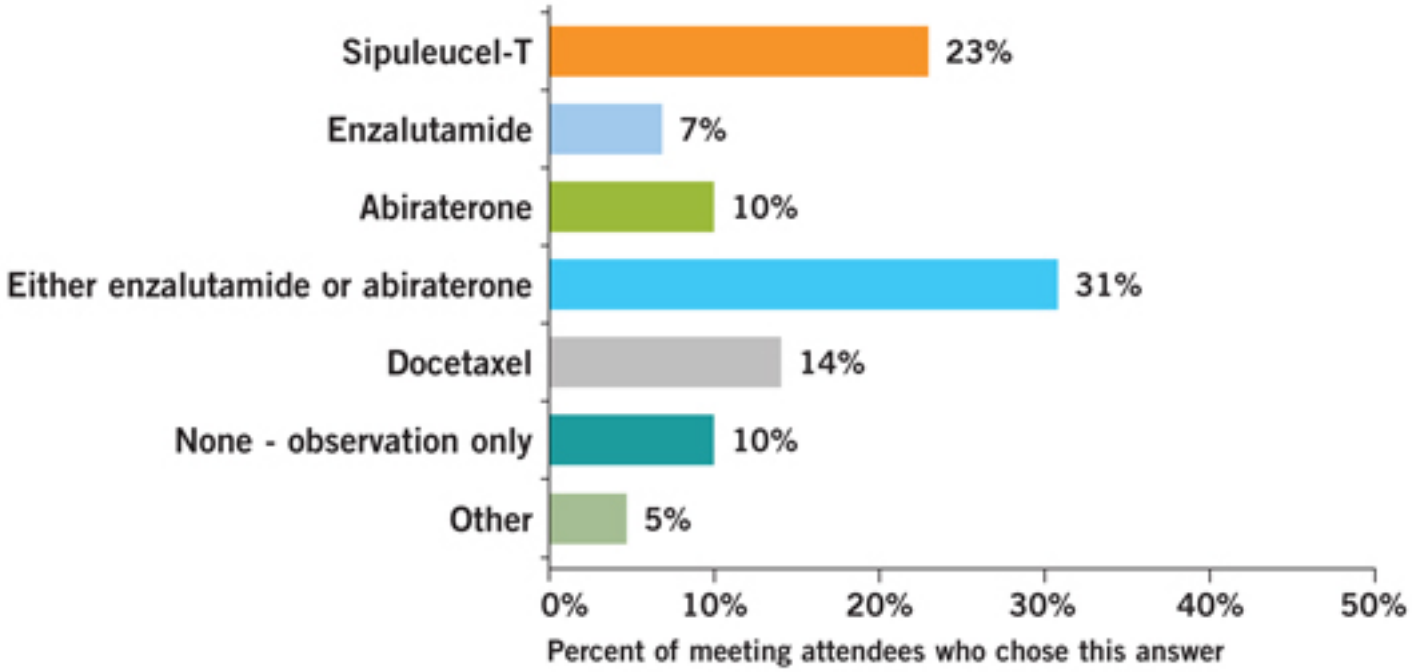
Year in Review

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

Endocrine and Bone-Targeted Therapy for Prostate Cancer — Charles G Drake, MD, PhD

A 60-year-old man presents with asymptomatic bone and nodal metastases that develop while he is receiving androgen deprivation therapy (ADT) for PSA-only disease. What therapy (in addition to bone-targeted treatment, if any) would you most likely recommend?



DR LOVE: Chuck, we presented to the audience a 60-year-old patient with prostate cancer who's getting androgen deprivation for PSA-only disease, a typical situation — now develops bone and nodal mets, but the patient is asymptomatic.

This is sort of the classic situation, which, if you're going to use sip-T, it seems like it would be here. And a fair number of people in this audience would use sip-T, but the rest would go on to hormonal therapy. How do you think this one through, Chuck?

DR DRAKE: I think this is a very fair representation in terms of the answers. If the patients are asymptomatic and have minimal disease, then I think that sipuleucel-T is probably an excellent choice. For patients who have more aggressive disease, the PSA is going up a little quicker, maybe a higher PSA, then I think the trend is toward using a second-line antiandrogen, particularly enzalutamide. I think both answers are reasonable. But one thing I would say is: If you're going to use sipuleucel-T, probably best to use it in this earlier setting rather than waiting until later in the disease course.

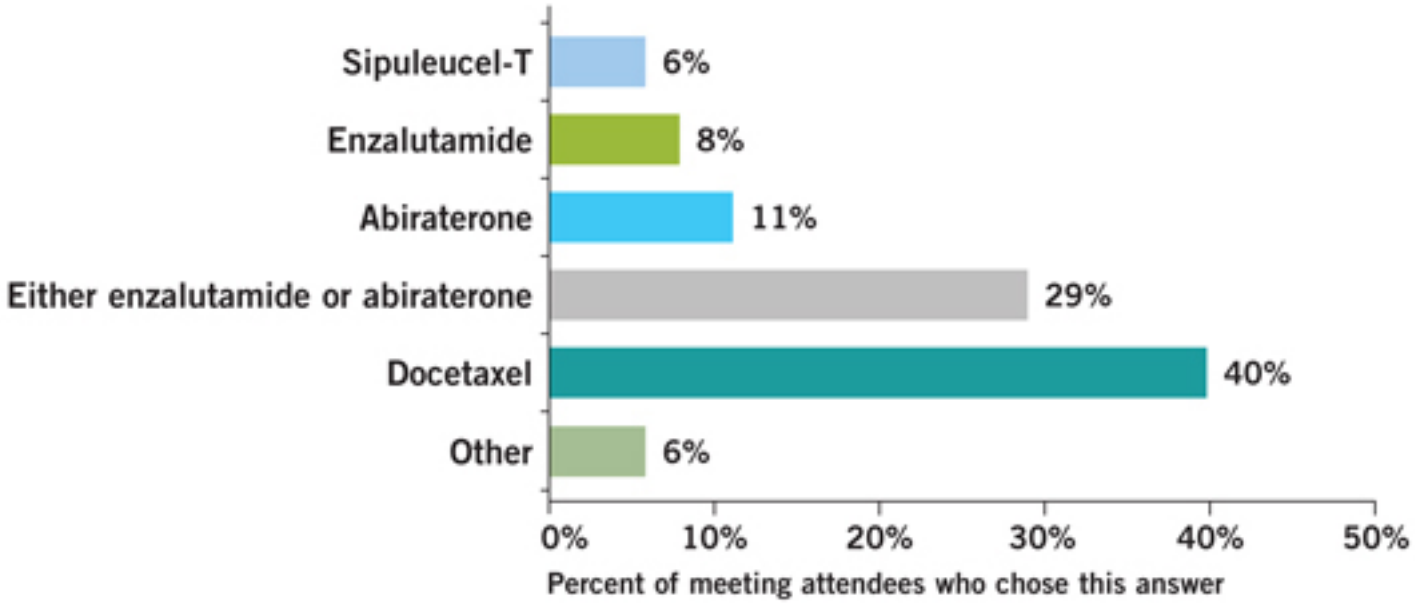
DR LOVE: William, you always want to see people's PSA go down. They start feeling better. We know that you don't usually see that right away with sip-T. Very tempting to go with a hormone. On the other hand, theoretically, they should have greater survival if you try the sip-T. How do you think about it?

DR OH: I think that exact way. If you're going to do sip-T, if you're a believer in sip-T, this is the time to do it, particularly if the PSA is not rising quickly and if the patient's truly asymptomatic. You remember, it only takes 5 weeks. So if you're going to do it, you do it. You make sure the patient understands his PSA may not go down. And I start to preauthorize them for abi and enza right at that moment because I know that we're probably going to have to line up the next treatment right after.

DR LOVE: But just to be clear, are you likely to use sip-T for this patient?

DR OH: I think I actually voted for either enza or abi, although I do use sip-T. I'd say I use sip-T in about a quarter of my patients in this setting. It goes to what Chuck was saying. Not everyone is a great candidate for sip-T. If their PSA is rising slowly, they're truly asymptomatic, they didn't have a particularly aggressive disease earlier, that's the type of patient that I would line up for sip-T.

A 60-year-old man presents with symptomatic bone and soft tissue metastases after receiving ADT for PSA-only disease. What therapy (in addition to bone-targeted treatment, if any) would you most likely recommend?



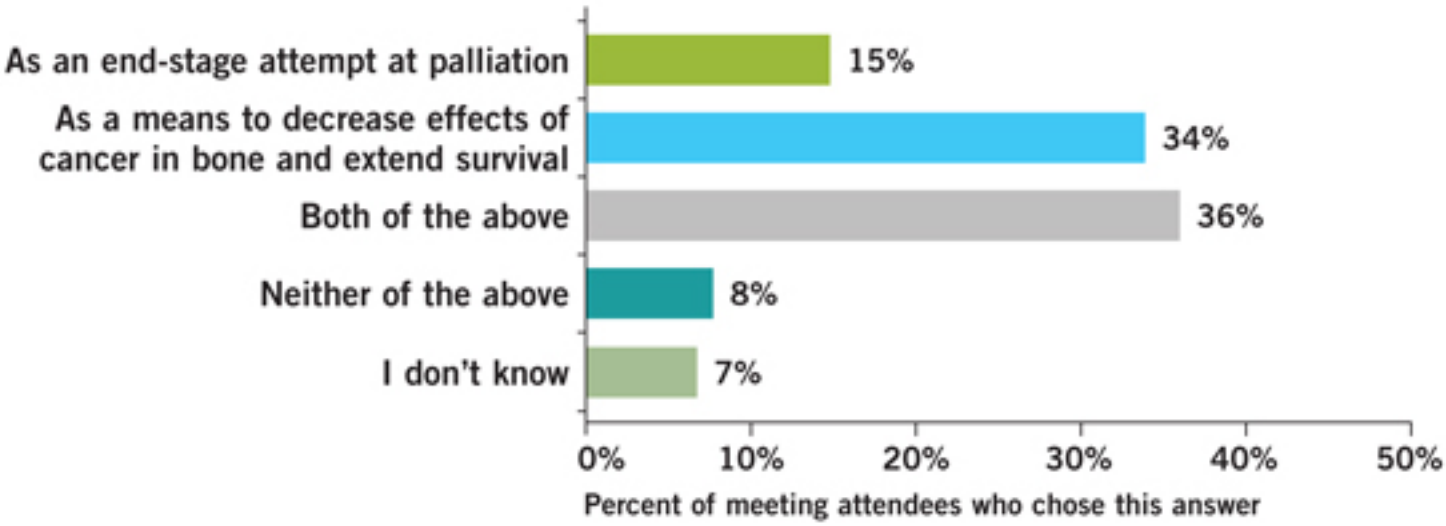
DR LOVE: Another issue is the symptomatic patient. Normally when we, Chuck, put this in there, change the scenario — now the patient's symptomatic — we start to see people using chemo. And you see that here. It's actually the most common choice. But I guess hormones are about the same. I think the implication, Chuck, is that maybe chemo would work faster or be more likely to work. And I'm not sure that's true. What do you think?

DR DRAKE: There are actually retrospective data published from COUGAR-302 and from some of the early enzalutamide trials suggesting that, really, chemotherapy and second-line hormonal therapy like enzalutamide or abiraterone are actually almost exactly equivalent in this kind of setting. They're published in a review that we put in *The Oncologist* earlier. It was surprising because there is this widespread feeling that, "Oh, man, if the disease is progressing quickly, you should think about chemo." But that's frankly not supported by the retrospective data that have been analyzed from the published trials.

DR LOVE: So, William, you have a patient that comes to you for a second opinion. The first doc has said, "Docetaxel." Do you say, "That's a reasonable option, but that's not what I do," or do you say, "I just don't think that's a good idea"?

DR OH: That's exactly what I say. I think it's an option, reasonable, but that's not what I do. Like Chuck says, I think there's a bias that chemo is going to be more active here. But we've all seen patients with very symptomatic disease respond. The most important thing is: What's going to work? And we know abi and enza both have very high response rates and value in this setting too.

How do you conceptualize the role of radium-223 in the treatment of metastatic prostate cancer?



DR LOVE: Chuck, I've been hearing about radium-223 now for a couple of years. Honestly, it's been kind of hard to tease out when you use it and what it's all about. I've given that a little bit of thought, and this is a new question we never asked before. I was talking with Oliver Sartor in Chicago about this idea that I wonder whether people really need to rethink what radium-223 actually is. Because, historically, we had samarium, et cetera, that was used, end stage, to try to palliate pain, but to me, as I've been thinking about how people have been talking about this, this is more like a debulking agent. If you have mainly bone mets or only bone mets, clinically you can reduce the amount of tumor like chemo, in a way, without any toxicity.

I thought that that's kind of what it is, which is option B. You see a diversity of opinion here. I'm kind of curious. I brought this up with you previously. Do you buy into the idea that this is really a systemic/survival kind of strategy?

DR DRAKE: Certainly it's systemic in terms of the way it targets the lesions in the bone. We know from clonality studies that lots of lesions come from existing lesions, from the genetic studies, mutational studies. So the idea is: If you can reduce the burden in the bone, you could extend survival and, in fact, debulk the tumor to some degree. I argue against that a little bit for the guys who just picked the first one. Most of the studies that we know, that have been published, have been in a later line of disease. I think some studies that are Phase II studies, that are in earlier phase of disease, that are actually accruing now, will help us to clarify that a little bit.

DR LOVE: William, there's not very much data early on. We just need a lot more data in general. But, in general, it seems like maybe it ought to be something that you think about, just like a noncross-resistant antitumor therapy, to try and get in there. I don't know. Do you buy into this sort of concept, William?

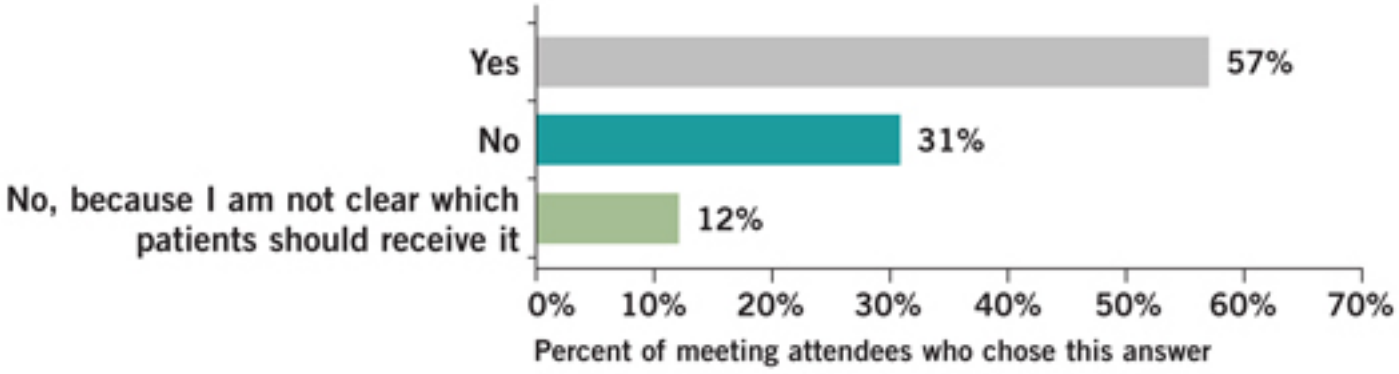
DR OH: I do, but I understand why people can't get their hands around radium-223. It's not a drug that traditionally works the way chemotherapy or the androgen-targeted therapies work. We like to see benefit in terms of real effects on patients, their pain going away, which it doesn't necessarily do, or their PSA going down.

I chose B as well, but what's interesting here with the answer is that people are still confused. I would say that choice C can't be possible, in a way, because if it's end stage and also extending survival, those seem at odds with each other. But I do think that it does extend survival. I do think that it's another option that extends survival. How it works, I think, has been the biggest problem for a lot of oncologists to really feel comfortable with.

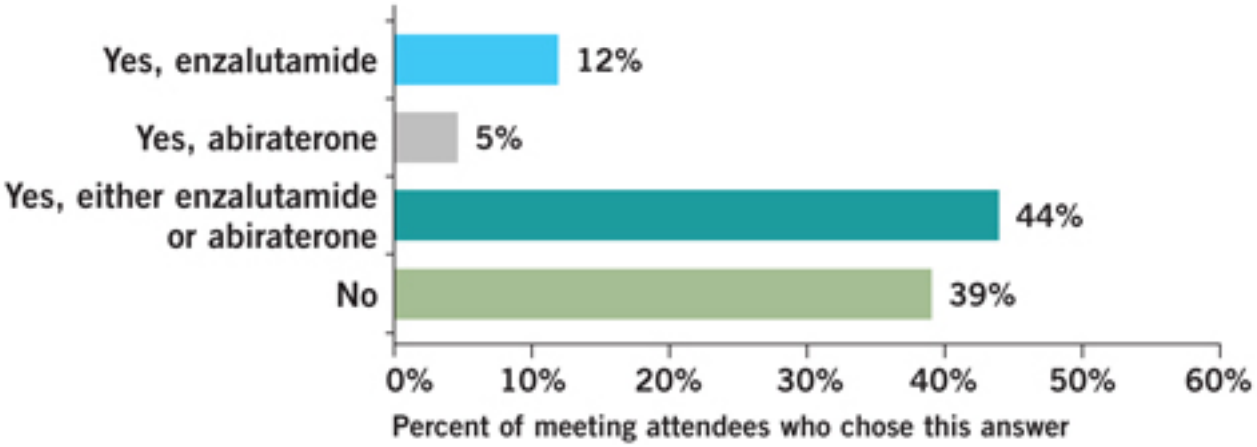
DR LOVE: What I've been hearing a lot about is combining it with abiraterone or enzalutamide. Is that kind of the way you're using it?

DR OH: I am because 6 months of a monthly radium is hard to leave a patient on unless there's clear evidence that their cancer is not progressing elsewhere. And so I am often combining it if it's possible from an insurance point of view.

Have you referred patients with prostate cancer for treatment with radium-223?



Cost and reimbursement issues aside, are there patients with PSA-only disease to whom you would administer enzalutamide or abiraterone?



DR LOVE: We don't have any data on these new hormonal agents, or maybe a little bit in PSA-only disease, yet we're using secondary hormonal therapy that we know is not as good. So why should we think about using it? Interestingly, in the audience a little bit more than 50% would like to use it. A bunch of people wouldn't. Chuck, what are your thoughts about this? If you could use it, would you use it in PSA-only disease?

DR DRAKE: Yes. Patients with a rapidly rising PSA, with so-called PSA-only disease, with conventional imaging studies that are negative, have metastatic prostate cancer. It's really a bit of an arbitrary detection based on conventional bone scan and CT scan. A patient with rapidly rising PSA who is a candidate for this, who's failed an LHRH drug, I think it is a very reasonable approach.

DR LOVE: I would assume, William, that for practical purposes it's impossible to get with PSA-only disease outside a trial, or can you get it?

DR OH: I think it depends on how strict their insurance company is. I've used it in this setting. I think a lot of times insurers believe that they're going to have to use this in advanced prostate cancer anyway, so we have been able to get it.

DR LOVE: And just to clarify, it sounds like chemo in this space is a little different story.

DR OH: I think we've never gone to using chemo in this setting. Some people, when docetaxel was first approved, thought about it. But I think the toxicity profile doesn't argue for chemo yet.