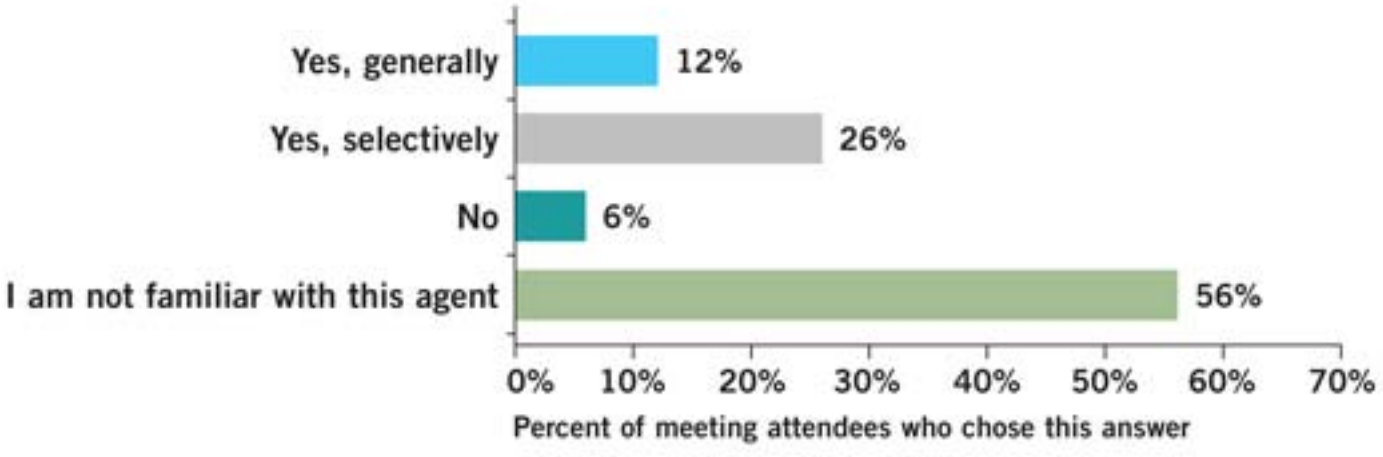
Year in Review

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

Hormone-Naïve Prostate Cancer and Novel Approaches to the Management of Renal Cell and Urothelial Bladder Cancer — William K Oh, MD

If atezolizumab (MPDL3280A) were granted a broad approval for the treatment of metastatic bladder cancer, would you use it as first-line therapy?



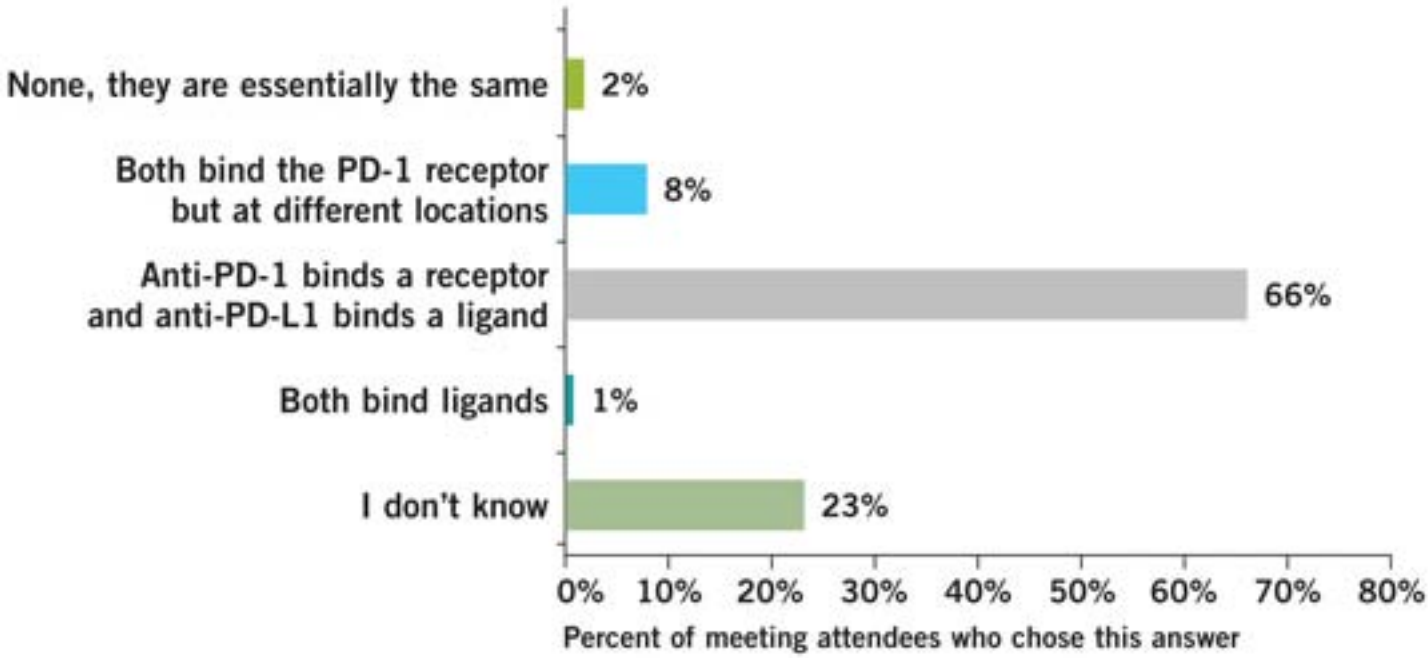
DR LOVE: I think last year at this meeting, I remember, for the first time, we started to talk about anti-PD-1, or, actually, PD-L1 in bladder cancer. I think we had Dan Petrylak here this year, who was the PI on the study. We were curious, first of all, whether people have heard about it. Now it's got a name. I don't think last year it had a name. But they always try to make them as hard as possible to pronounce. In any event, most people aren't familiar with it. This one seems, William, like it's going to be really primed. It's the PD-1+ story.

I'm curious, Chuck. Based on the responses that have been seen, it seems like it ought to be available. If you had a patient with this, I would not want to see them die without somehow either getting this on a trial or et cetera. How do you think it's going to become approved, Chuck, and would you ever use it first line for an older patient you don't want to give chemo to?

DR DRAKE: I think that based on the nonrandomized, large Phase II study done with 300 patients, recently completed, that it will get accelerated approval for bladder cancer. So it'll be out there.

That study was done in the second line or the platinum-ineligible population. So, frankly, first-line platinum ineligible will be included in that group of patients. For platinum-eligible patients, it does look like the prior treatment might upregulate the immune response, might upregulate PD-L1. So if patients are eligible for platinum, it might be that the drug will work better in the second line, actually. We don't really have those data, but the trial was second line or first line, if platinum ineligible.

What is the difference in the mechanisms of action of anti-PD-1 and anti-PD-L1 antibodies?



DR LOVE: In terms of the difference between anti-PD-L1, which is what [atezolizumab] is, and what we hear a lot more about, which is anti-PD-1, I was curious whether this group was aware that they have a different mechanism. The drugs like atez get the ligand, like bev gets the ligand, for example, and PD-1 goes after the receptor.

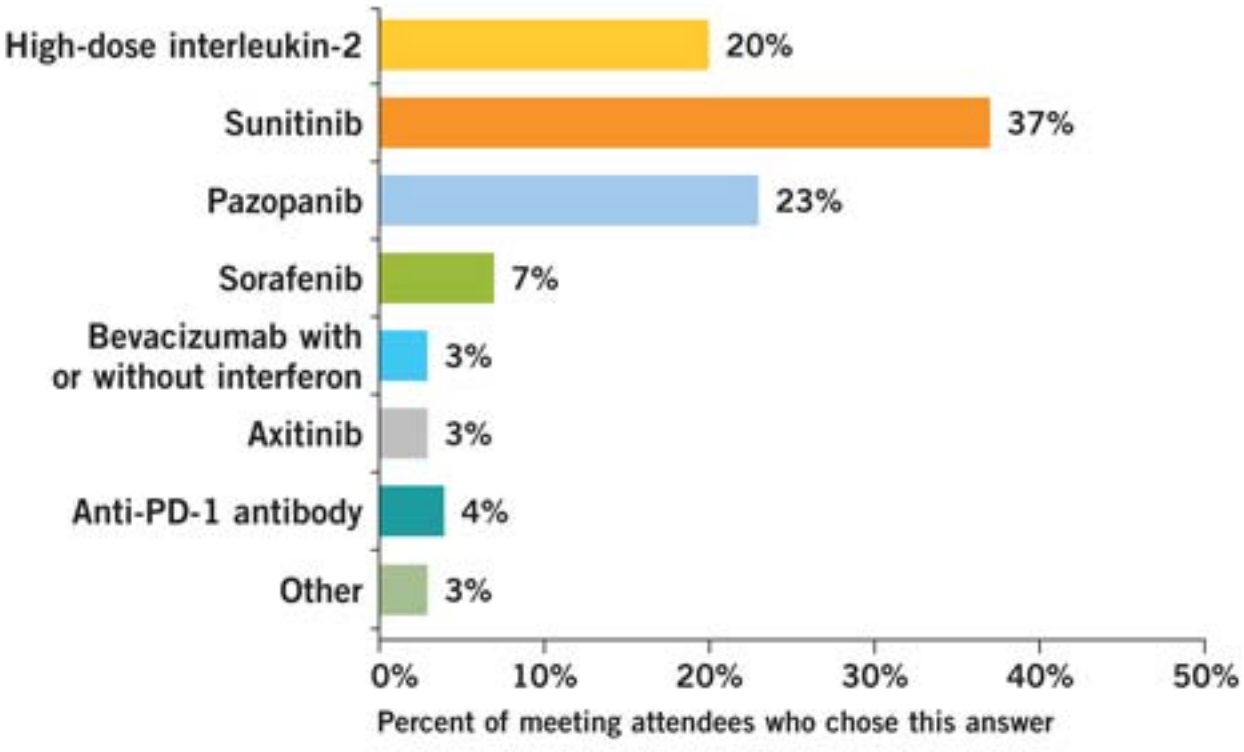
DR DRAKE: Correct.

DR LOVE: What are the implications? Clinically they seem very similar.

DR DRAKE: PD-1 is on T cells, and it turns them off, right? Its ligand, PD-L1, is on tumor cells or other cells. But there's another ligand. There's PD-L1 and PD-L2. The anti-PD-1 antibodies block both those interactions. They stop PD-L1 or PL-L2 from hitting the PD-1 on the T cells. Theoretically, they could be more potent, and they could have more side effects.

The interaction of PD-L2 with PD-1 also turns off the T cells, but it might prevent autoimmunity. Theoretically, antibodies that block only the PD-L1, like atezolizumab, would allow that PD-L2 to turn off some T cells through PD-1 and could be better tolerated.

Cost and reimbursement issues aside, in general, what is your preferred first-line systemic treatment recommendation for a younger (age 55), otherwise healthy patient with metastatic renal cell carcinoma (mRCC)?



DR LOVE: Another PD-1 issue that is coming up very rapidly is renal cancer. We asked the audience, William, about their first-line therapy today, assuming you could access everything. We were curious whether anybody would think about it first line. Nobody would think about it first line. A little bit more sunitinib versus pazopanib. How do you make the decision, William? I hear people saying sunitinib/pazopanib, equal efficacy, pazopanib, better tolerated.

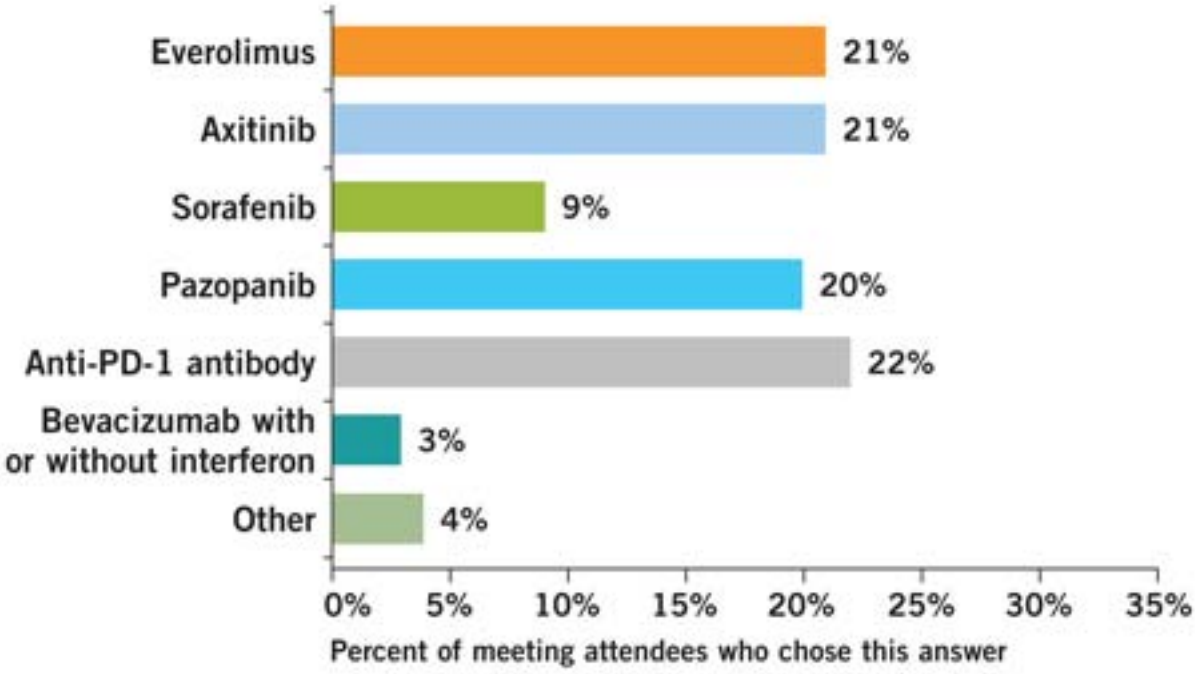
DR OH: I use pazopanib for that reason, but, of course, I started with sunitinib, like everyone in the audience. I think people feel comfortable with what they start with, and that may be driving that. What shocks me about this is high-dose IL-2. I guess that's always a question of whether there's a referral center nearby that gives high-dose IL-2.

DR LOVE: Chuck, what would you like to get if it were you?

DR DRAKE: I agree with William on pazopanib. There was some data from a Phase II trial of anti-PD-1 in kidney cancer that suggested the first-line response rate might not be as good as the second- and third-line response rates. So I really think that currently pazopanib is probably a good choice, or sunitinib.

Now there is an ongoing trial that completed accrual in the first line with immunotherapy, but that doesn't look at nivolumab alone. It looks at nivolumab plus anti-CTLA-4. In the first line, you might need something a little stronger.

Cost and reimbursement issues aside, in general, what is your preferred second-line systemic treatment recommendation for a younger (age 55), otherwise healthy patient with mRCC who initially responds to sunitinib for 7 months and then experiences disease progression?



In patients with mRCC, the combination of lenvatinib and everolimus resulted in prolonged overall survival compared to...