

## BroadcastMed | cmr\_8932\_intereactive\_question\_and\_answer2-1080p.mp4

SPEAKER 1: So now, we're going to have the interactive dialogue session. We have questions. Again, if you have questions, put them on your question cards. I'll grab them, and I'll tee them up for the panel here. So here's the first question that's come in. Are we close to predicting who will have the durable response among these? Do we have any idea from this yet, or will we need more studies to take a look at that?

**SPEAKER 2:** Well, what we're really seeing here in some of the data that comes out from the initial melanoma experience is, the answer is yes, but. Yes, those patients who have a significant partial response or complete response are the ones that we're associating with a long durable response. We're understanding that the majority of patients who achieve a complete response maintain that, just like Dr. Lewis's patient.

That there is a subset, 20%, 30% of patients who get a partial response who are going to progress in the future, we have to have an answer for. This idea of stability of diseases come under fire now, because we're seeing that that durability may not be as great as the others. But as far as knowing the number that you're going to have this type of response, aside from having a PD-L1 staining, high mutation alone, we have to do better with these predictive markers.

So what I tell patients is that you have an equal-- even if your PD-L1 levels are low, you have a chance of having a response rate that is durable. And as your response evolves, we can talk about what's coming up next. I always discuss the fact that the majority of these breakthroughs have come through clinical trials. And those will be there at progression for an evaluation.

**SPEAKER 1:** OK. Carl, any comments?

**SPEAKER 3:** I agree with what was said. We don't have predictive biomarkers yet. I don't check PD-L1 status on any of my patients, because I don't use that in terms of treatment decision making. It's clear that patients with high PD-L1 expression are likely to do better, but you can't use that as a negative test. People who don't express PD-L1 won't respond to immunotherapy. So we don't have that upfront biomarker.

In terms of patients who do respond, it's those patients like the case that I showed, that had a very rapid and meaningful response. They're the ones who are most likely going to maintain that. So we can get those clinical clues. But we don't have a biomarker in that situation, either.

**SPEAKER 1:** I think to me, when I look at this, it's somewhat analogous to melanoma. That's the slide that we showed earlier with [INAUDIBLE] about the seven year, phase one follow up for PD-1 for nivo and melanoma. And you see that everybody who survived for three years pretty much went beyond it. You look at Jimmy Carter, right? Who is a 90-plus year old with melanoma. And that's in the brain. Normally, you'd think he had extremely poor prognosis, yet he's still alive. And he was on nivo, I understand. So the bottom line is, maybe we'll get to this point with this drug for squamous cell carcinoma in terms of advanced. But I don't think we just have a follow up to look at that yet.

**SPEAKER 3:** That's correct. [INAUDIBLE] There's some hints on that progression free survival curve that I was pointing out that it's starting to plateau. And we're hopeful that's going to be durable. But we need the longer follow up to do.

**SPEAKER 1:** OK. So next question is, in people with squamous cell carcinoma who are undergoing treatment with biologicals for conditions such as RA, can they receive the immunotherapy modalities that are discussed today? Or do they need to stop their other methods while the skin cancer is being treated?

- SPEAKER 2:** I'll take that. We're finding that more and more that we can treat these patients. In a clinic such as ours, we try to minimize the immunosuppression as much as possible. And then, the experience has been that you can treat these patients. It's about 50/50 whether it exacerbates their condition. But at the same time, what you're dealing with is a life threatening condition. So we have extensive discussions with our patients. And then move forward.
- SPEAKER 1:** And I think that's a challenge. Certainly what's interesting about this class of drugs is that it does have less major adverse effects as some of the other drugs we use for various things. I know there was just a case report about using PD-1's in a woman who was pregnant with melanoma. And in fact, she had metastatic melanoma and did quite well with it. So just in the New England Journal, I think a couple months ago, with it. But Carl, comments?
- SPEAKER 3:** When people come in with underlying autoimmune disease, as we said, you have to balance that risk benefit ratio. These patients by and large do have life threatening malignancies. And that often overrides things. So it's how severe is the autoimmune disease? If it's something like rheumatoid arthritis, which is they have an exacerbation, it's not going to necessarily be life threatening. And it will be, certainly, a morbidity. But somebody who has severe Crohn's disease-- that's something else. So you have to take those things into consideration. But we do treat patients, routinely, with underlying autoimmune disease with these drugs
- SPEAKER 1:** OK. The next question is-- this is actually, we don't have surgeons here, officially. But, what role do wound care doctors play in helping with healing post-op wounds while the patients are on treatment or have completed treatment? Are there any issues with using the state of things that might be used, like an apligraf or epigraf grafts into the products of right, whether they're hydra gels? As many of these products have growth factors, would that affect the treatment of these wounds as they're healing, do you think?
- SPEAKER 2:** The answer is, we don't know. Most likely not. I try to keep anything that is necessary on board and anything that's unnecessary off. There is no clear data in this realm. So I would say if it's a wound that needs to heal, you go ahead and treat it. Treating with the PD-1 will cause tumors to regress and help with the wound healing.
- SPEAKER 3:** These are not chemotherapeutic drugs. So there isn't any wound healing issues with the drugs themselves. So somebody who has a bad wound, putting them on a PD-1 antibody is not going to hinder the ability of that wound to heal.
- SPEAKER 1:** OK. And then, a question about the cost of the therapies. And are they typically covered, in your experience?
- SPEAKER 2:** So that's a great point to put out here, that they are covered. This is an FDA-approved drug. And the indication there is for these patients with locally advanced and non-resectable. So the answer is, yes, they should be covered by all insurances, as they are FDA-approved. Now, if you go off label and treat with something else, then you're exposed. So this has an approval. It has a J code. It has everything necessary for you to order it, as we have, and give it to the appropriate patient.
- SPEAKER 1:** Do you have the same experience in Colorado also with this?
- SPEAKER 3:** Yeah, we don't have any issues getting the approval.