SPEAKER 1: All right. So we're going to leave you a summary of the program with you, what we tried to show you today. And basically, the idea behind this was to give you information on these new therapeutic options and try to determine which patients might best benefit from using a PD-1 checkpoint inhibitor.

Again, reminding you that there are over 3 million non-melanoma skin cancers in the US. About 600,000 plus of those are squamous cell carcinoma newly diagnosed each year and that the number is probably higher than that for a variety of ways.

We talked about the fact that there are probably more deaths than we think about. Certainly in the southern part of the US there's as many deaths from squamous cell carcinoma as there are from melanoma in that area.

We talked about the JAD guidelines that exist. And they came maybe a year ago but, in fact, this is really not covered in them because it's such a new area of discussion and focus on squamous cell carcinoma sighting area.

In terms of therapeutic options, we spoke about the pathways that are involved here and the importance of the PD-1 inhibition for this, the likelihood that, in fact, you would see an increased response to a PD-1 and PD-L1 blockade for this type of approach with objective responses.

We spoke about the rationale for PD-1 inhibition in cutaneous squamous cell, the fact that if you look at the median numbers of somatic mutations, you see that, in fact, it's elevated for a cutaneous squamous cell compared to a lot of other solid tumors. Of course, the FDA has just newly approved cemiplimab for this application in terms of advanced squamous cell.

This is the article that came out recently in the New England Journal looking at the data. We viewed that data with you-- the fact that the majority of patients in the phase two study did respond and had stable disease subsequent to this, the fact that the overall survival rate among the patients in this phase two study who had advanced cutaneous squamous cell.

In fact, about 50% of the patients did have progression free survival with that, just subclinical showing the fact that the tumors do shrink. At least these are two examples from the New England Journal article for this, which shows impressive. And finally, where are we going in the future with this? I think that's the most exciting thing. How are we going to identify those who are going to respond to PD-1 blockade?

We talked a little bit about genetics, maybe genetic expression profiles. We have models to look at this. We're not there yet. We need to better identify these patients. What are the reasons that people fail this yet? Well, some of it we just don't know yet.

We're sort of attacking broadly and hoping to get a percentage. But we have to develop more targeted ways to determine this. Will we be able to develop other immuno-inhibitors? What's the reason that some immune cells fail to infiltrate the tumor? What's the tumors defense?

We don't totally understand all of that yet. We don't really have any good neoantigens at this point. What are the mechanisms of secondary failure to respond? which is important too. And what about expression of other immunoinhibitory receptors? We need to identify that and loss of MHC.

So I think these are the questions of the future. Do you want to add anything? [INAUDIBLE] you think where we're going in the future with the challenges we have?

SPEAKER 2: No. I think you've done a great job pointing out that what we are taking back to our colleagues into our clinical trial program in order to find these answers-- what's important for us now is to grab the tissue and the tissue-- the tissue at response at progression and to evaluate in real time what's happening there. So it's not a static thing that's happening to these patients in these tumors. It's very dynamic. And we have to understand the time course of that dynamic response.

SPEAKER 1: And I view this analogous somewhat with BRAF and melanoma. If you have a BRAF mutation, you know that the BRAF inhibitors are working. If you don't, it won't work. We really don't quite have that yet, I don't think.

SPEAKER 2: Right. And then as those BRAF inhibitors stop working, there are secondary mutations of resistance that we're finding. And we're finding that there are certain people who have specific mutations that respond even better to immunotherapy and have a shorter response duration to BRAF inhibitors, so the same idea for immune therapy.

SPEAKER 1: And Carl, beyond these, where do you think we're going?

CARL: Well, from a general standpoint, it's been a very exciting last number of years where immunotherapy has been taken out of the realm of melanoma. Melanoma and kidney cancer was where immunotherapy was being used and now it's in lung cancer, bladder cancer, triple negative breast cancer.

So the changes have been rapid. But there still is a lot to be learned. Why is primary resistance to immunotherapy there? Patients do develop secondary resistance to immunotherapy-- what immunomodulating agents do people need in trying to identify those markers is the area of active research. But it's been an exciting time.

SPEAKER 1: OK. Well, basically concluding what we talked about today-- generally, squamous cell is a good prognosis but locally advanced and metastatic disease can develop. And that technically not has a good prognosis. There's been previously little effective options. Chemo really hasn't worked well.

Targeted therapy has some benefits. But this is really a new exciting area of using PD-1 and antibodies such as a cemiplimab, which is now approved. It's really a major step forward. And still we need improvements. We don't know all the issues with organ transplant patients.

And the response rate is not 100%. So there's room for growth in the future. But this is an exciting step forward, I think, to really make a difference and have other options that are armamentarium for our patients with us. So we're going to do some post-program assessment questions.

And if you wouldn't mind, we're going to do-- these are follow-up questions when we asked you at the start of the presentation today. So first of all, based on engaging with the CME symposium, how likely are you to employ PD-1 inhibitors for the management of patients with advanced unresectable and metastatic cutaneous skin cancers?

[MUSIC PLAYING]

OK. Results. Well, clearly that's moved up from what we saw early on. OK. Next question. This is based on your engaging with the symposium your current level of clinical knowledge as it relates to the use of PD-1 inhibitors with advanced unresectable and metastatic cutaneous SEC is-- what do you think your level of engagement-- level of understanding, rather, from the symposium?

[MUSIC PLAYING]

OK. Results. So it's clearly moved up a little bit from what we saw before. OK. Next question. And this is basically the same question. How about your knowledge as it relates to clinical trial data and comparative mechanism of actions and the implication for management for these advanced SEC patients?

[MUSIC PLAYING]

OK. Results. All right. So that's clearly moved up from the initial. Some knowledge has been gained from the initial questions. OK. Question four. This is based on your information from the symposium. What about your knowledge and comfort level using PD-1 inhibitors in appropriately selected and screened patients with advanced SEC-- has increased, increased clinically meaningful, significantly, or has remained unchanged.

[MUSIC PLAYING]

OK. Results. OK. At least everybody's moved up somewhat. That's always the goal for any kind of educational activity. So that's great.