Getting Ahead of irAEs: Fostering Change in Structural Systems for Disadvantaged Populations

Ticiana Leal:

Hello. I'm Dr. Ticiana Leal, and on behalf of CME Outfitters, I'd like to welcome you to today's educational activity, titled "Getting Ahead of Immune-related AEs: Fostering Change in Structural Systems for Disadvantaged Populations. Today's program is supported by an educational grant from Bristol Meyers Squibb and Merck Sharp & Dohme corporation. Today's activity is brought to you by CME Outfitters, an award-winning, jointly accredited provider of continuing education for clinicians worldwide. I also want to encourage everyone to join us on Twitter. Let me now introduce our panel for tonight. I'm Dr. Ticiana Leal. I'm an Associate Professor in the Department of Hematology/Oncology. I'm Director of the Thoracic Medical Oncology Program at Winship Cancer Institute of Emory University, in Atlanta, Georgia. Joining me today, Dr. Aung Naing, Professor of Investigational Cancer Therapeutics at the University of Texas MD Anderson Cancer Center, Houston, Texas, editor-in-chief of the *Journal of Immunotherapy* and *Precision Oncology*. We also have with us today Dr. Kristen Whitaker, Assistant Professor in the Department of Medicine, Georgetown Lombardi Comprehensive Cancer Center, Washington Hospital Center, Washington, DC.

Our learning objectives for tonight's activities include to recommend improvements to structural systems, to better support immune-related adverse event management in historically disadvantaged patient populations. So, as you may have seen in the first two parts of this series, cancer disparities exist among many populations. Disparities are a complex mixture of factors, such as socioeconomic, for example, including access to insurance, geographical, community setting, education, attitudes, and conditions within the health care system. So tonight we'll be discussing immune-related adverse events associated with immunotherapy, including immune checkpoint inhibitors. We'll discuss approaches to recognizing and managing immune-related adverse events, and also how disadvantaged populations are at risk, or higher risk, of poor outcomes when they experience immune-related adverse events. I'd like to ask Dr. Naing and Dr. Whitaker to say hello, and then Dr. Naing, you've been at the forefront of immune-related adverse event management. Could you tell us a little bit about immune-related adverse events to lay the groundwork for the discussion, following your introduction and hello to our participants today?

Aung Naing:

Hello everyone, I'm Aung Naing. I am glad to be joining here today. Dr. Whitaker?

Kristen Whitaker:

Hi, good afternoon. Good evening. I'm Dr. Whitaker, and I'm pleased to be here tonight. I hope you guys find this to be a very informative session.

Aung Naing:

Thank you, Dr. Leal, for the introduction, and also posing the questions. I'd like to start giving the definition of what immune-related toxicity is. Whenever there is a disruption of homeostatic mechanism, and then with that, we see the unique spectrum of the side effects. This is coming from the immunotherapy and that is the immune-related toxicity. And we call it irAEs. If you look at the literature, you might see the irAE ranging from 70 to 88%. That is, we are talking about all grades. And if you look at anything above grade three and above, you can see five

to 25 patients--of those patients who receive the immunotherapy. So you see there a wide range of the number. The reason is, it depends on what type of the treatment these patients are receiving, what type of the immunotherapy, and whether they are receiving as a single agent monotherapy, or they are getting the combination.

So depends on that. For example, patients who are getting the combination, you might see more of the immune-related toxicities. Now let's look at some of those immune-related toxicities. The most common immune-related toxicity is the dermatitis, and then followed by the enterocolitis, hepatitis, and endocrinopathies. But by far, the most common reported irAE of any grade, all the way from one to the higher grades, that is the dermatologic toxicity. So why is it important to understand immune-related toxicity? The patient may have a very low grade, like a grade one, but if we do not recognize, and if that is left untreated, those grade one can rapidly progress to two, three, and eventually it can go all the way to the life-threatening conditions, and even, it may be, further. So what is really important here is A, you recognize the immune-related toxicity early in the game, when it is in the low grade, or when it is really early beginning of those immune-related toxicity. Recognize and treat, so that you can actually slow down, and then you can take care of those patients.

And then I'd like to also look at the mechanism of immune-related toxicity. There are several mechanisms of those underlying immune-related toxicities. The very first one is a one-hour day's breach of self-tolerance. If you remember, when we are doing the immunotherapy, we are reprogramming, reeducating, reactivating our immune system. For example, we have got naive immune cells, and then those naive immune cells, you have got a T cell diversification that can lead to the B cell diversification. With that, you can have autoreactive T cells or those autoantibodies formations. That is the one mechanism those autoreactive and autoantibody can elicit immune-related toxicity. And the second mechanism is what we call cross-antigen reactivity. So we have had that antigen that is sitting on the tumor, and then also that is sitting on the normal tissue. So something like on the skin. So because of that, there is a shared antigen that is on the tumor and on the skin, and with that, you can also have an immune-related toxicity.

Another thing that we also see is because of the cytokines' and chemokines' production, you know what we are trying to deal with those innate immune system or adaptive immune system, they're going to produce cytokines and chemokines, and hopefully that way we're targeting the cancer cells. On the other hand, it could have also impact on the normal tissue, such as the heart or the kidney. Another mechanism is that we call it off target effects. For example, you see the CTLA-4 sitting on the pituitary gland, and you give the anti CTLA-4. There is a potential impact of the effect on the pituitary gland.

So we talk about the breach of the sub-tolerance of cross antigen reactivity. We talk about the effect of the treatment production, or the cytokines and chemokines. We also have to remember the microbiomes, because there are microbiomes sitting in every part of our body. And then what we know is that these microbiomes can produce pro-inflammatory cytokines, and then that can also lead to the immune-related side effects. So that is where we are with the mechanism, and of course, I'd like to also ask Dr. Whitaker whether there are other facts, when we are talking about the immune-related toxicity.

Ticiana Leal:

So Dr. Whitaker, can you comment on the data that we have for other groups? Gender, ethnic, and age differences in the incidence, or in the severity of adverse events? How did the data that we have guide us here?

Kristen Whitaker:

Yeah, so I think one of the big challenges that we face when we look at our understanding of immune-related adverse events is that if we realistically look at the clinical trials which led to the approval of these agents, like the checkpoint inhibitors, less than 5% of those patients were from underrepresented minority groups. So we know very, very little from the clinical trial data about what differences we may see in African American or non-white patients, for example, and the other population that was not very representative in these clinical trials also were older patients. So again, we have very limited data to say whether we expect worse or similar outcomes in different non-white racial groups and older patients.

We extrapolate from what we know from some of our chemotherapy agents. We do know that, especially with certain chemotherapy agents, sometimes older patients are more prone to have adverse events. And we also know that some minority patient populations can have more severe adverse events. But I think right now we have very limited data. We need more studies that really include a representative patient population when we look at these agents, and we need to continue to use real-world data on adverse events to really help guide our understanding here.

Ticiana Leal:

Great points. Now, next let's next move on to a polling question. So before we get into further discussion, particularly in the underserved population, let's take this question that I'll read to you, and then please take the time to respond and answer the question. How confident are you in promoting structural changes that mitigate care disparities for patients receiving immunotherapies? Not confident at all, somewhat confident, confident, extremely confident. Okay. So the majority, 53%, said not confident at all. 35% said somewhat confident, 6% confident, and 6% extremely confident. Thanks everyone for participating in the polling question. So let's move on, and I'll ask Dr. Whitaker to talk a little bit about the guidelines, the ASCO guidelines, for managing irAEs. Dr. Whitaker?

Kristen Whitaker:

Yeah. So this is just an overview, and hopefully provides just a very practical approach, but it's good to remember that when you're managing your patients with immunotherapy and they have toxicity that there is many, many resources. But ASCO has nice clear guidelines for management of these immune-related adverse events. So I think the very, very first point to note here is that it's very important that clinicians are able to accurately grade the immune-related adverse event, because it makes a big difference in how the treatment or management is guided. But if you have a grade one adverse event, the reality is that you don't change therapy much. You monitor the patients closely for the most part, but they continue with their treatment. For grade two toxicities, it's important to remember that close monitoring, and continuing therapy is not appropriate. In grade two, then you really have

to hold the immunotherapy, and consider resuming when the toxicity reverts to grade one or less. Most times for a grade two immune-related adverse event, you're going to need to administer corticosteroids.

We have the dosing here, but it's normally somewhere between 0.5 and one milligram per kilogram, per day of prednisone. And then when we think about our more severe grades of these toxicities, so grade three and grade four, grade three, again, it's important to remember, just like with grade two, you're going to be holding the treatment at this point, and you're going to be administering corticosteroids for these patients. In some patients, corticosteroids may not be enough, and you may have to move up to treatment such as infliximab. And again, similar to grade two, once you do these steroid treatments and the toxicity reverts to a grade one or less, you can actually rechallenge. So that's an important point. Just because you have a grade three toxicity, if you treat the patient and they actually improve and go back to a grade one, you can resume the immunotherapy. But it's important to remember for this most severe or grade four, which is really these life-threatening and very serious immune-related adverse events, normally permanent discontinuation of the immunotherapy agent is recommended.

Ticiana Leal:

Let's move on to our next point of discussion, action items, and how these action items can potentially address these issues of disparities in cancer care. Dr. Naing?

Aung Naing:

Thank you. I had the privilege of working on these action items, proposing these actions items together with my colleagues. And I think the very first thing is educating our patients, and our caregivers. And also, some of our patients will be also treated by the health care providers from the different subspecialties, such as in the emergency room, or primary care physician, or... So I think it's educating our patients, caregivers, and health care providers is really critical. And also we talk about, we have got the IIA management guidelines. They are out there from the ASCO and also ASMO or SITC, but there is also a need how we can refine those irAE management guidelines. With that, what is also important is how we report those immune-related toxicities. So that could be a standardizing reporting system, and one of the things that also we need to be aware is, we use immunosuppressive agents, but what immunosuppressive agent would be optimal and how we can optimize our choice of immunosuppressive agents. In order to do so what we also need to do is, this field is evolving. Our understanding of the immune-related toxicity is quite evolving.

So we need to pursue better understanding. If we want to better understand, we need to also include those high-risk patient populations, which we will discuss later. And Dr. Whitaker also has more what we mean by the high-risk patient population. And then again, at this time, it's also important to understand the value of those diagnostic clues, and to incorporate these diagnostic clues, particularly when we are going to personalize immune-related toxicity management. We now have wireless technology, and how we can use such wireless technology and digital health while we are managing our patients. One of the things which is really critical is we do everything, but the most important question is what the patients wanted to tell us. How they are feeling, and how they are going through. So I think providing a platform to hear the missing patient voices is critical. And then we are learning, and if we don't share, people are not going to understand what the other side is doing. So it's so

important, any knowledge that we are gaining, we should be sharing with the community so that we can all get benefit from the collective effort.

Kristen Whitaker:

Now I wanted to move into just talking to you a bit about some of these action items. What are some of these practical approaches that we can take and we can implement now. So, like Dr. Naing said, I think one of the most important ways that we really can ensure that all patients, regardless of their race, regardless of their age, regardless of their gender, have optimal outcomes from these therapies, and are able to stay on these therapies, and get the benefits that we know they have, is it really starts with educating the entire team, as well as patients and caregivers. So when we think of how we want to do this, in the past, there was a more paternalistic approach to medicine, where we would say, "I'm the provider, you as the patient, you need to do this."

We really want to facilitate a communication pattern where patients and providers are really sharing information. Patients have trust in their providers. Patients understand actually the treatment that they're given, and what to expect in terms of side effects. So really this more collaborative team approach to the care, I think is really critical when we're thinking about how we best address disparities, and potentially outcomes from different patients using these therapies. But I think sometimes people ask, “Well, what is something practical that I can do?” And I think one of the simplest ways to improve outcomes, potentially, in patients, is something that we've used at institutions I've worked at in the past, are our patients on immunotherapy, they get what are called these drug wallet cards, essentially. So immunotherapy wallet cards, which I'll talk about again in another slide.

But the idea is that it's the card that you give to the patient at the beginning of their treatment, and with that card, you say, this is the agent that I'm on. This agent can cause these specific side effects. And it really is designed not to be used within the oncology setting, but to be used, if a patient, for example, shows up in the emergency room. You should really be instructing your patients, okay, you have this card, keep it in your wallet. Now you're in the emergency room, give it to the doctor. And normally on the card, it says, my oncologist's name is this. Please call them at this number to discuss my case. I think that's one way to make sure all patients, regardless of their health literacy, can communicate what therapies they're on, and have their providers contacted to appropriately co-manage patients, even when they're not in the oncology setting.

And then we'll talk about some of these things too, as the night goes on, but there are also now several educational apps that explain more about immunotherapy side effects, about how we can monitor for some of these side effects, patient brochures, and different things like that. And then I think probably one of the most important points, since we really are focused somewhat on how do we mitigate these disparities in outcomes for patients getting immunotherapy, it's really important when we're talking about education that we really are tailoring patient education resources to the health literacy levels of the patient, to also reflect the individual cultural needs of the patient, as well as their emotional needs. So really this tailored patient education is key.

Aung Naing:

Thank you, Dr. Whitaker. We also mentioned previously about this irAE management guidelines, we are fortunate to have several guidelines out there. I mean, from the ASCO, NCCN, SITC, and SBO, if you look at these guidelines, more or less, they are the same. There may be some level of a difference, but what we really need to do is though

this area is evolving. The way we manage our patients with the irAE is truly evolving. And then what we need to do is though, we have to make sure that we continue to update how we are going to take care of our patients. We need to get the input from multiple specialties across all the health care providers, how we are going to manage when we are seeing a patient. Because there will be some patients they may not be seen by the oncologist. They may be seeing in the emergency room, or they may be seen in the primary care physician's office.

So getting those input, and then making sure that we keep updating, and then that has to be a regular plan effort. It is also important to bring those, how we are going to manage an unrepresented patient population. So there should be an effort to redefine how we are doing so that we can improve in what we are taking care of our patients. So one of the thing is that when we are reporting the immune-related toxicity, we normally use, in oncology, anytime we are treating our patients, either with the chemotherapy or immunotherapy, targeted therapy, we use CTCAE criteria. It's a great way, the way that we communicate to each other, "Hey, I have a patient, your patient, I am seeing here in the emergency room with the grade two immune-related toxicity of the colitis," and the other physician on the other line of the phone would understand what this patient is going through.

So CTCAE is our universal language when we are trying to talk about the side effects, but unfortunately CTCAE does not capture all the immune-related toxicities. For example, when you look at the CTCAE criteria, particularly when you have a patient with a skin toxicity only immunotherapy, you find it inadequate. So what we need to do is we need to actually incorporate those irAE into the CTCAE criteria, and they say actually ongoing effort. And I think what we need to do is making sure that those CTCAE criteria reporting will capture the side effects caused by the immunotherapy, so that we can communicate with each other more effectively and clearly.

Kristen Whitaker:

And now I just wanted to, again, just give you a little bit more information about what we can do to really try to improve screening and identification of irAEs early on, to ensure that, again, all of our patients have the best outcomes. So we talked about it in a prior slide, but I think honestly, one of the easiest ways that we can start improving outcomes among all patients, again, regardless of their education, or health literacy level, or access to care, is to really provide these immunotherapy wallet cards to patients. So again, this is a card that really the patient could fill out themselves, but I actually think it's probably more helpful if the care team, so the health care team, actually fills it out and gives it to the patient, or if they fill it out together. But it's an easy resource to give to patients.

And again, while oncologists may be quite familiar with how to manage immunotherapy adverse events, it's been shown time and time again, that in certain community settings, in certain emergency rooms, primary care offices, that same comfort with managing immune-related adverse events is not there. So involving the patient's oncologist really, I think, is a key step in terms of improving outcomes. So I think I put here a couple of resources for where you can get these immunotherapy wallet cards, but in reality, they are very simple. I think that any community practice, any institution, could actually make their own specific immunotherapy wallet cards. So I think they are easy action items to implement. And then I also think another way that we potentially improve outcomes of our patients with immunotherapy, without relying on the patient to do the work, is again, implementing things such as electronic medical health record alerts, where essentially if a patient shows up in the

emergency room, when that patient shows up, there's a banner that comes up on the patient's chart that says this patient is on this immunotherapy agent.

And then at least there's a understanding of this is an agent that may need some higher level of management, or consultation, or something like that. But I think these immunotherapy wallet cards, it's really a key and easy implementable strategy moving forward. And then I think the other way, when we think about how do we, again, make sure that all patients are having the best outcomes when they're on these agents? I think the key to this, we've seen this time and time again when we look at cancer treatments that are not immunotherapy, but just chemotherapy and surgery and radiation, we know time and time again, that when we standardize treatments for patients with cancer, and ensure that black patients, white patients, older patients, younger patients get the same treatment, we know that they have better outcomes. And most cases where disparities existed, for example, in things like breast cancer, they no longer exist when we standardize the treatment approach. So thinking along those same lines, it's very important if we want our patients to have the best outcomes, to really standardize their screening, as well as the coordination of their care.

So I really think in every oncology clinic, when these patients are on these agents, there should be some standardized screening measure that is being done in the clinic. I don't think this necessarily has to be done by the physician, but I think this could be something that's done by the nursing team. And once that assessment is completed, it should be documented in a standard way, and then how you manage should almost be an algorithm. If you have this pop, then the oncologist does this. If you have this result, an oncologist does that, or the nurse does that, but I think standardization is really key. And it also should be done in a somewhat standardized screening timeframe. So it's not really helpful if in one clinic, a patient is getting screened with these questions once a month, and then in another clinic, they're getting screened with these questions once every six months.

So I think we really need to come up with a timeframe that's appropriate for patients on certain agents to have screening done. And then I think a key, key point, again, I think if we want our patients to have the best outcomes, then we really have to work very hard as providers to standardize the coordination of care. So really have the patients knowing exactly who to contact if they have problems, whether that's a triage phone line, whether that's the nurse, whether that's the physician's call line directly. But then also having the nurse know exactly how to navigate the patient through the system, if issues may arise.

Ticiana Leal:

Dr. Whitaker, there's a really interesting question that came from our audience, talking about the role of the multidisciplinary team, and perhaps this is a good point to comment on the role of the pharmacist, the role of the nurse, the role of the entire multi-D team in helping patients manage, and to bridge the gap.

Kristen Whitaker:

Yeah. So I think in terms of the pharmacist, I think specifically they asked about the pharmacist, I think where pharmacists really become very helpful is with really helping with understanding once you have this grade, how we then manage the toxicity, and things like dosing and dose reductions. I also think that a lot of programs actually have, institutions will actually have, pharmacists that help participate in some of the toxicity monitoring

for some of these agents. I think that's a little bit of a harder ask, I think, depending on the time and resource allocation of the pharmacist, but I think that can be helpful.

But I think in general, I don't think it can be one model for every type of institution. I think we really have to think about your individual resources you have, but understanding that with what resources you have, you have to make sure that every member of that team has a clear understanding of what their role is, in terms of one guiding the patient to report their side effects. But two, once side effects, adverse events are reported, what role they play in the management of that. Because I think pharmacists play a role in that, I think nurses play a role in that, and definitely the physicians play a role in that as well.

Ticiana Leal:

Great. Thanks for that response. So moving on to our next slide, we talked about how we have guidelines from ASCO, SITC, ESMO, and many others to help us guide our patients in terms of managing and treating immune-related AEs. But we also know that some of our data is extrapolated from non-cancer data, and not immunotherapy, mainly from the transplant setting. And so I think one of the things that we talked about earlier is, how do we manage immune-related adverse events and how do we personalize it? Let's have Dr. Naing take over and talk about optimizing choices, and how do we move forward?

Aung Naing:

Oh, thank you, Dr. Leal. Yes. Right now, most of the time when we have a patient with the irAE, we use steroid. Steroid is actually the very first line type of the treatment. So using the steroid, high-dose steroid, for longer duration, I mean, it comes also, we have to pay some price for that, because of the steroid use, you could have potentially some of those side effects coming from the steroid. So I think what we need to know is though, if we understand the mechanism, whether this type of the side effect is actually mostly driven by the antibodies, or T cells, or cytokines, that area, that understanding, in fact, is evolving. And then in that way, we can be actually more focused, in this type of the irAE, this is the driving mechanism, and this will be better immunosuppressive agent.

So I think that level of the understanding is so crucial for us. And then we need to do really a prospective studies to understand once we know that, hey, how safe this immunosuppressive agent is and how effective it is when we are managing the irAE. And also we have to remember that we need some level of the immune activation to fight the cancer. So what is the impact? Because we are using the immunosuppressive agents, are we also losing the effect of the immunotherapy when we are controlling the cancer? So we need to actually optimize our choice. What dose are we going to use, and how long are we going to use? I think those are the areas that we need to do better. We need to understand better. In that way, with a better understanding, we will be able to in fact, manage our patients better.

We now actually know that if we use the same drug, two patients may have the same type of tumor. They're almost the same age, the same race, and the same sex. But despite the fact that everything looks the same, but you might see one patient may have a grade one colitis, and the other patient may have a grade three colitis. Why? And sometimes you may have a grade three, but one has got the colitis, and the other one has got dermatitis. Even though everything looks the same, the drugs and the tumor, the age, and sex, and the race. And

then sometimes you might see that one patient may have a grade one colitis, and the other patient may have a grade three pneumonitis. So we still are trying to understand why everything, even though it's the same, they have different types of the reaction.

So that means that what makes some patient more susceptible to some irAE, is there any role of the organ specific or tissue specific immune microenvironment that is contributing to the irAE? So that's also important to understand, whether it's a germline genetic variation. That's why you have got the different types of the irAE. How about, are we having a shared expression of the antigen between the tumor and normal cells? The one that we just discussed earlier, we see that vitiligo in the patients with the melanoma. So our opinion is that we need to have a good knowledge about the immune effect or pathway that is driving irAE. If we have a better understanding of these pathways, then we can use immunosuppressive agents better that is more appropriate for that. There are things also we need to know, what is the relationship between having the immune-related toxicity, and response to the immunotherapy?

There are some literature out there these days, for example, we are using vaccination. What is the risk and effectiveness of the vaccination in those patients when they are getting the immunotherapy? And as Dr. Whitaker said earlier, we are using the steroid, for example, for the grade three immune-related toxicity. We might have to use on a longer duration. At that time, we have to also start thinking about the prophylaxis. So what are the concerns about those opportunistic infection when we are using the long term steroid used? And of course, we always need to have a greater inclusion of the non-white patient population, and then so that we can have a better and comprehensive understanding of the immune-related toxicity. So, another thing which is also important is that we talk about the high-risk patient populations. So far, we are trying to understand how to manage our patients who are at the high risk. Who are the high risk? For example, a patient who has got a kidney transplant, or organ transplant patient who have stem cell transplant for their disease.

How about the patients when they have got the preexisting autoimmune disease history of the rheumatoid arthritis or SLE? There are also patients with the primary and secondary immune deficiency patients, for example, HIV positive patients. They may be prone to get the Kaposi sarcoma type of the cancer. So patients with a history of the HIV, Hep B, Hep C, and then also those patients who received the immunotherapy in the past, and they have gotten some immune-related toxicity, and they came up. Now, most of the time, in many of those clinical trials, these patients may be excluded from participating. I think it is important to understand how are we going to take care of our patients who have got the high risk? And the best way is that we want to make sure that when you encounter those patients, make sure that you refer those patients to the appropriate tertiary cancer center, where they are running the clinical trials, so that these high-risk patients are managed through the clinical trials. And Dr. Whitaker, could you also include about those underprivileged patient populations?

Kristen Whitaker:

Yeah, I mean, I think that we know that some of our minority patients have more comorbidities that could complicate their treatment from immune-related adverse events. So just keeping that in mind, too, when we are treating these patients, I think becomes an important point here.

Aung Naing:

Thank you. So one of the action items that we have laid out earlier is how we are going to use the diagnostic clues. Today, when we are treating the patients, we know that there are some biomarkers that we know that some of the patients could be responding to their treatment, such as if you have got the PDL1 positive, or if your tumor mutation pattern is high, then they were likely to respond to the treatment. Or if you have the microsatellite instability is high, we know that those patient could benefit from the treatment. However, when it comes to the immune-related side effects, we still are in the area of trying to get better understanding. I think biomarkers are quite important, and there are actually certain studies out there, they are trying to identify what biomarkers can be used to predict the risk for the immune-related toxicity.

And the reason is that we need to have a better understanding of these biomarkers and their relationship to predict who is going to have a response. So the onset response, who is going to also have a risk for the immune-related toxicity? So it's important to identify, and then we need to develop some tools to monitor these patients. If we know that this is going to be the biomarkers that could be associated with the immune-related toxicity, then if there is a way that you monitor those patients. We will have several biomarkers, but what is also important is to validate these immune markers in clinical tools. In order to do so, we need to conduct large and prospective studies that will bring us a more reliable, and then that can be used in the general population. So those are the things we think we need to be doing to take care of our patients.

Ticiana Leal:

Dr. Naing, one of the questions that has come up regarding biomarkers, you're mentioning that we should develop these, are these ready for prime time? Are there any currently clinically available to help us risk stratify patients at risk for irAEs?

Aung Naing:

Thank you, Dr. Leal. There are a lot of efforts going on, however at this time, there is no validated biomarker that we will be using, if you have got this biomarker, you're going to have a higher risk. So having that, however, the scientific community, oncology community, is working on that to identify who is at the high risk, using the several biomarkers, and even including the patient reported outcomes, to understand who are at higher risk of getting the immune-related side effects.

Ticiana Leal:

Thank you.

Aung Naing:

And thank you. And to continue with the discussions, we are at the era of the wireless technology and digital hub. And in fact, what we have being doing in this area is, for example, we have got the IOx management apps. This is an app where you can download on your iPhone or Android. We actually have this app, we use CTCAE criteria, and we use ASCO guideline from the first publication. And then by doing so, anyone with this Android, iPhone, can

download such apps. Please remember though, when you use these apps, they are actually talking about how are you going to manage through the guidelines.

Guidelines are so general, here you have got the patient in front of you. You use the guideline to take care of the patients. So please make sure the guidelines are the guidelines, the patient in front of you is your real patient to use such guidelines. So I think there is a technology out there such as IOx management or some of the acute oncology apps. But however, we have to also understand that how we can have this type of the apps available to beyond the tertiary cancer center. And Dr. Whitaker, would you like to add on that?

Kristen Whitaker:

Yeah, I mean, I think one of the big things when we think about utilizing digital health for our patients is, while it really has the potential to revolutionize how patients report information, actually allowing providers to get that information more quickly, it also stands to really dramatically worsen disparities, if we don't have a way to ensure that all patients are equally able to access these tools. So I think we all sit and we think to ourselves, well, everyone has a smartphone. The reality is, studies have looked at this, and about 40% of patients don't actually have smartphone access. So when we look at who those patients are, they're more likely to be patients of lower socioeconomic status. They're more likely to be older patients. So these are two patient populations that already stand to potentially have worse outcomes from their cancer. So we want to make sure if we have these apps, that everyone can access.

So one, making sure that patients have access to smartphones or computers. Two, that they have internet access to use these devices on their smartphones. But I think one point that we didn't emphasize as much on the slide, but I think it's critically important is that we also have to make sure not only can patients access these tools on their phones, they have to understand how to use them. So, I mean, they use this term called “digital literacy” to essentially describe that not only patients can access the information, but they can understand and navigate the app once they get into the application. And I think that digital literacy piece is what we cannot forget when we start really implementing these in our patient populations.

And just like health literacy varies across different racial and ethnic groups, different education groups, different age groups, we're going to see the same thing with digital literacy as we continue to study it in a health care setting. So I think if we're using these devices, making sure we have the proper resources to really make sure that once patients access them, they know how to use the tools. So I think for some patients that's really going to be making sure that there's some dedicated person that sits down, whether that's a nurse, it's probably not going to be the physician, again because of time, but whether it's a nurse or some other care coordinator in the clinic. So again, where this care coordination really becomes important, it's going to be key here when we start to move into really utilizing some of these tools.

Aung Naing:

Thank you. And so we also previously talked about hearing the missing voice from the patients. We know that those patients who actually report their symptoms, they have, in fact, when you look at some of those published data, they have got the better outcomes, but the question is how we can actually hear those missing voices. What are the challenges to hear their missing voice? And Dr. Whitaker, would you like to add here?

Kristen Whitaker:

Yeah. So this was actually an interesting study that came out of Memorial Sloan Kettering, which essentially was really just trying to look at the benefits of this proactive monitoring of patient-reported symptoms, to see if when patients report symptoms, does that actually improve outcomes? So specifically when they report symptoms earlier. So with this tool of reporting symptoms earlier allowing the clinician to intervene earlier, we actually saw that patients had improved overall survival. So again, this really just speaks to this point of really, when we're dealing with our patients, and especially on these therapies that can have so many adverse events, that we really should make sure that we're emphasizing to patients that one, they need to know what symptoms to look out for. And two, they need to know when to report the symptoms to the health care provider. So we always say that when we talk about patient reporting, we tell our patients report early and report often about their side effects. And we know that actually does help in terms of their overall survival. And then-

Ticiana Leal:

Dr. Whitaker, some of the slides over the next few are a recap. Let's move on to the next few slides. We're coming to time, so I'd like to leave room for a thank you at the end. And thanks for summarizing the next few slides for us.

Kristen Whitaker:

And just very quickly, because we are short on time. I think this is an important slide for you to know about some of the resources for patients. I know someone asked the question, well, what resources can we use for older patients, or for patients who can't use digital technology? I think simplified, print educational materials are still probably the best action for those patients. Here are just some of the examples. Everyone may not be aware, but actually all of the big cancer organizations actually have educational guys, ESMO, ASCO, NCCN. So you can go to their website so you can actually print these out. I think it's a good idea to print them out and actually give them to patients, rather than relying on patients being able to access them once they leave the office. And then again, this is a similar idea, but just this idea that we really want to have a very collaborative approach that encourages the patient to know their side effects, and to voice those side effects so that we really can manage their adverse events appropriately.

Aung Naing:

And I would say that we are learning, but unless we share, we may not be able to advance the field. So what is very important is to share the data. Whatever the data, clinical translation into the scientific community in a timely manner is really important. That will enhance our communication, and our management skill when we are taking care of the patients.

Ticiana Leal:

Thank you very much. Thank you, Doctors Naing and Whitaker for the very interesting discussion. And I'll summarize some of our key highlights of our presentation and discussion today. So to summarize, we want to increase immune-related adverse event awareness through education, solidify the irAE management guidelines, acquire knowledge by performing preclinical, translational, and clinical studies in diversified populations, including

a broader population and real world population and trials, and share the knowledge gained. And before we continue, let me take a moment to wrap up this portion of this activity with our smart goals, which are actions we can take into the clinic starting tomorrow morning. So our SMART goals: specific, measurable, attainable, relevant, and timely. To deliver culturally sensitive patient education, tailored to the needs and capabilities of the patient and the caregiver, encourage the call early and call often, as we discussed, approach to symptom reporting. Maintain a low threshold for suspecting irAEs in patients receiving immunotherapies, and review the grading of irAEs in order to personalize management.

To wrap up, please remember to receive credit, you'll have CME credit for this activity. The participants must complete the post test and the evaluation online. Please download and print your certificate immediately upon completion. So our time is about up. I wanted to thank Doctors Naing and Whitaker for joining me this evening. It's been a very interesting conversation on a very important topic, and I think we could go on and on because there's still so much to talk about, but I also want to thank our audience. Thanks for joining us, thank you for sticking with us till the very end. And lastly, please go ahead and visit the CME Outfitters Oncology Hub to access additional activities on relevant oncology topics, and the diversity and inclusion hub for discussion of disparities in health care, as well as resources and patient education materials. Thank you everyone, and have a good night.