Dr. Stukus: Hello, and welcome to Conversations From the World of Allergy, a podcast produced by the American Academy of Allergy & Immunology. I'm your host, Dave Stukus. I am a board certified allergist and immunologist and serve as the Social Media Medical Editor for the Academy. Our podcast series, we use different formats to interview thought leaders from the world of allergy and immunology. This podcast is not intended to provide any individual medical advice to our listeners. We do hope that our conversations provide evidence-based information. Any questions pertaining to one's own health should always be discussed with their personal physician. The Find an Allergist http://allergist.aaaai.org/find/ search engine on the academy website is a useful tool to locate a listing of board-certified allergists in your area. Finally, use of this audio program is subject to the American Academy of Allergy, Asthma & Immunology terms of use agreement which you can find at http://www.AAAAI.org. Today's edition of our "Conversations from the World of Allergy" podcast series has been accredited for continuing medical education credit. The American Academy of Allergy, Asthma & Immunology is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Information about credit claiming for this and other episodes can be found at https://education.aaaai.org/podcasts/podcasts. Credit claiming will be available for one year from the episode's original release date. Today we are pleased to welcome Dr. Julie Wang who is a Professor of Pediatrics at the Icahn School of Medicine at Mount Sinai in New York. Dr. Wang is heavily involved in both clinical care as well as clinical research at the Jaffe Food Allergy Institute. Dr. Wang's research interests center on understanding the epidemiology management and novel therapeutic options for food allergy. With almost 100 peer reviewed publications and extensive involvement within the American Academy of Asthma, Asthma & Immunology, Dr. Wang is an accomplished academician and a perfect guest for today's episode which will discuss peanut oral immunotherapy. As disclosures, I have served as a consultant for Aimmune sponsored non promotional educational activities. Dr. Wang discloses relationships with the following companies that have developed therapies for peanut allergy. She's a member of the DMC for ALK-Abelló, has research grants for food allergy from DBT Technologies and Aimmune and serves on the Advisory Board for DBV Technologies. And with that, Dr. Wang, thank you so much for taking time to join us today and welcome to our show.

Dr. Wang: Thank you, it's my pleasure to be here today.

Dr. Stukus: Well I think this is going to be a great conversation and as we'll get into, it's very timely as well. It is for CME credit but I think we're going to have a wide ranging audience that are going to be interested to hear what you have to say. So let's start with some basics, help us all understand the scope of peanut allergy as we stand today in 2019, what does this look like, how many people are affected, are we seeing rates that are rising and if so, the million dollar question, why is that?

Dr. Wang: Yeah, that's a great question and it's on the minds of many patients, families as well as us in the healthcare world. This is a very important issue these days, recent estimates show that just over two

percent of children in the U.S. have peanut allergy and this translates to nearly a million and a half children and teens in the U.S. and so there is data to suggest that there is a rise in the number of children being affected by peanut allergy over recent years, as much as a threefold increase in a approximately ten year timeframe.

Dr. Stukus: Do we have any idea why we're seeing such an increase in rates of peanut allergy?

Dr. Wang: So that is a million dollar question, there are a lot of theories as to why that's happening, one of the prevailing thoughts has been the timing of exposure of peanut to our young infants which stems from the data that came from the U.K. looking at rates of peanut allergy in Israel versus the U.K. and correlating that with the timing of peanut exposure in those two places which ultimately led to the LEAP Trial that was published in 2015 showing a significant decrease in rates of peanut allergy for the infants who are high risk who were randomized to introduce peanut early in life. So the timing of exposure of peanut allergen to young infants who are at risk seems to play a big role however that probably is not the entire answer because data from the LEAP study also show that by the time they we were screened for that study there were already about ten percent of kids who showed evidence of peanut allergen sensitization meaning that they were potentially allergic even before the four to six month age frame. Also there were kids, a minority granted but there were some kids who were randomized to receive peanut early in life yet still ultimately developed peanut allergy. So some other ideas as to why this is happening is the way we're exposing people to peanut. So typically we think about allergen exposure to foods by mouth, however for young kids with eczema, allergen exposure can occur through the inflamed skin and exposure through that route can potentially skew to a more allergic profile.

Dr. Stukus: So it sounds like the way that we're feeding infants is a big part of the problem but there's no clear one reason or one answer why. And I don't know how many times a day you get this question but I get it quite frequently from parents, especially grandparents who say, "Nobody had peanut allergy when I was a child," but I think it's important to kind of have that conversation with folks and let people know there's no clear cut reason why.

Dr. Wang: Right. This certainly isn't something that parents should feel guilty about because it very likely is going to be multifactorial, not only the timing of peanut exposure but whether there are other medical issues such as the eczema that I had mentioned. There may be also other factors that were just not well understood right now because there are many other theories that are being explored.

Dr. Stukus: I love that you said that there's a lot of guilt out there and it's not your fault and I think that's a message that all of us can tell mothers because I know that a lot of parents have that unnecessary burden of thinking that they did something that caused their child's peanut allergy, so thank you for saying that. Now you mentioned millions of children, two percent of the population of the United States have peanut allergy, that's a lot of kids that need to avoid peanut but walk us through a scenario of daily life, what does life look like for somebody who has a peanut allergy and also if you could address what situations really place them at greatest risk for experiencing allergic reaction?

Dr. Wang: Yeah so food allergies, specifically peanut allergy is something that is not outwardly visible to people outside the patients and their family and so in some ways it's very difficult for non allergic patients and families to truly understand the impact the diagnosis has. And so the primary management strategies that peanut allergic individuals need to take is that they need to take steps to make sure that their food does not contain peanut because if they are inadvertently exposed to peanut, there is a potential for allergic reactions that can range from mild to severe including life threatening anaphylaxis. And so we eat all the time, every single day and so while it may sound fairly simply to just check your food and avoid peanut, it actually turns out to be something that peanut allergic people have to really think about throughout their day every single day. So one of the key things that we teach patients and their families is to read ingredient labels to ensure that whatever prepackaged foods that they're consuming don't contain the allergen and fortunately there are labeling laws in the U.S. that mandate clear labeling of peanuts as well as other major allergens if the food in fact does contain peanuts. What makes it a bit more challenging is that a lot of companies also use precautionary labeling which is also known as may contain or was processed in a factor and those statements are unfortunately not regulated and there is no good information for the consumer to truly understand whether those statements really indicate risk and if so to what degree of risk they are alerting the consumer to. So I've just mentioned the prepackaged food and that certainly is not the entirety of the food that we eat every day. We eat food in our own homes, we eat at other people's homes, outside in restaurants and so steps that can be taken in those scenarios would be clear communication. So this is a diagnosis that we encourage patients and families to not be shy about, anyone they interact with certainly around the food setting should know about the allergy and should understand the importance of having the food free of peanuts. And there are nuances of this again which the allergic individual knows very well but the non allergic person will not be thinking about so carefully. So for example when we talk about no cross contact we mean that not only is the dish not made with any ingredients containing peanuts but it should be prepared in bowls and using spoons that hasn't been used to stir in other pots that might have contained peanut because even small amounts are potentially able to trigger allergic reactions. So allergen avoidance is one key aspect but we know that things happen in real life and despite the best of intentions with reading ingredient labels and communicating clearly the presence of the allergy, mistakes can sometimes happen. And so the other main arm that we teach patients in terms of management is to always be prepared to treat an allergic reaction because there is no reliable way for us to predict when a severe allergic reaction can occur and so that entails the person carrying an epinephrine auto injector at all times because we just never know when we're going to get hungry and want to eat something and that carrying of the auto injector is also a constant reminder that potentially very serious life threatening things can happen. So there is a significant amount of work and burden that patients managing peanut allergy have to deal with as well as their families.

Dr. Stukus: It sounds like a lot of work, do families who have children with peanut allergy have heightened levels of anxiety as well?

Dr. Wang: Yes, that's a great question. There is data to show that patients with peanut allergy do feel more stress and anxiety as a result of their peanut allergy and this level of stress and anxiety is actually comparable to other chronic illnesses so this is a significant part of what patients have to deal with.

Dr. Stukus: And you mentioned focusing on trying to make sure accidental ingestion doesn't occur but what about other types of exposure, can someone get a peanut allergy playing Little League or go to a ballpark or fly in an airplane, is that safe for them to do?

Dr. Wang: So one of the main points that we educate patients and their families about is that the route of exposure that is most concerning to us is oral so meaning that the food allergen gets into their mouth via food or via transfer from biting their nails or sucking their thumb, I'm referring to young kids there. But contact and being around others who are eating peanut are considered very low risk scenarios. So there have been studies where there are simulated scenarios of a peanut allergic person having peanut put on their skin and/or being around others shelling peanuts or consuming peanut butter showing that those in fact are low risk scenarios for the patients. And one age group that requires a little bit more watchfulness is the young children, infants and toddlers where there is a lot of hand mouth behavior and that could be just hand in the mouth and/or mouthing toys where what would have been a skin contact exposure for an older individual, the allergen could be transferred to the mouth in which case an allergic reaction could occur in that scenario.

Dr. Stukus: So I've heard you describe now really a lot of nuances that surround various situations and individuals' risk for reaction, things like that and along those lines, does everybody with peanut allergy are they at risk for having a life threatening reaction from say a trace amount or do we see variability in sort of the amount of peanut somebody would need to be exposed to to cause a more severe reaction?

Dr. Wang: Yeah, that's a question on everybody's minds who is managing peanut allergy. So unfortunately right now there is no great test or way for us to identify individuals who are at high risk for having severe reactions with very small exposures. From oral food challenge data we do see that there is a range amongst the peanut allergic population where some people would have symptoms is very small, those exposures whereas others will have higher thresholds before triggering an allergic reaction. That is the food challenge which is a very monitored circumstance and unfortunately there is also no data where people undergo repeated food challenges, so we don't truly know whether if one is a high threshold reactor at one food challenge whether that threshold is maintained throughout multiple food challenges within a couple of days or weeks or months timeframe. So that is why we counsel all our peanut allergic patients to be vigilant so once you're diagnosed with peanut allergy the same level of vigilance and care is expected and advised for families.

Dr. Stukus: That's a great way to summarize that and it's challenging because we're stuck right, we have this natural variability but we have no way of identifying who really is at risk from these small amounts. And just to clarify because I hear this all the time where people are told from their say peanut skin prick test or peanut blood level that their test results indicates that they have a life threatening peanut allergy, is that the case at all?

Dr. Wang: Right, that's a very important point that we always teach our families is that these skin tests and the blood tests while they're good to some degree, they're not perfect and they don't actually provide us with as much information as we would hope that it can provide. So what these test results indicate is how likely the allergy exists so with higher blood IgE levels or larger skin tests we're more convinced that

the allergy exists, however these test results do not reliably tell us what symptoms would occur if an allergic reaction were to happen nor would they tell us how much allergen would be needed to trigger an allergic reaction. And so there is a lot of research right now to look at these types of questions and hopefully identify biomarkers which can provide this type of individual patient level information.

Dr. Stukus: What about the two percent of children that have peanut allergy right now, does that turn into two percent of adults that have peanut allergy or is it possible for somebody to naturally develop tolerance over time?

Dr. Wang: Yes, so fortunately we do see that some people can outgrow their peanut allergy, it is about 20 percent based on some data which is not the majority but there is hope for a subset of peanut allergic individuals to develop tolerance naturally over time. So we do expect that the adult population may have a bit less peanut allergy compared to children however there isn't great data at this point to know what the true prevalence of peanut allergy is in adulthood. The other tricky thing about understanding the rates of peanut allergy in adulthood is that there are some proteins in peanut that look very similar to tree pollen and so oral allergy is a potential issue for a lot of adults and we commonly hear this with apples, so someone who's had seasonal springtime symptoms for several years may find that they start having itchiness of the mouth and throat area after eating fresh apples but they can easily drink apple juice or eat apple pie without an issue. So this issue is called pollen food syndrome or oral allergy syndrome which is due to the homology between the specific protein and fresh fruits that come from trees and an analogous thing can be seen for peanut, so it is possible for some adults to have peanut allergy but in this oral allergy way as opposed to the classic IgE mediated allergies that we see in childhood. So for adults it's probably a combination of both.

Dr. Stukus: That's really interesting and I'm really glad you circled back to the IgE mediated food allergy because that's really what we're talking about here. So before we go any further, I just realized we haven't really described what that means, what kind of symptoms can occur when somebody has an IgE mediated reaction to peanut?

Dr. Wang: Right, so IgE mediated allergy really are immediate symptoms after the peanut exposure. So typically after ingestion we would expect symptoms within minutes to about two hours but unlikely to be several hours later and the symptoms can range really affecting any body system, often people think about skin symptoms such as hives, itchy rash and that is the most common symptom however allergic reactions can occur without skin symptoms. So other symptoms that can be seen in an allergic reaction include vomiting, diarrhea, nausea, respiratory symptoms such as cough, wheezing, trouble breathing, it can also show up as cardiovascular symptoms and that can manifest as feeling dizzy or pale or weak, low blood pressure. So a variety of symptoms can be seen in an IgE mediated reaction to peanuts.

Dr. Stukus: And to help folks understand context, you mentioned that typically these are going to happen pretty fast within a few minutes or up to a couple of hours after eating because these are some common symptoms that can occur for a whole host of other reasons so is that some of the education that you recommend that providers give to families about really putting it in that framework?

Dr. Wang: Yes, absolutely, the patients really need to understand what types of symptoms they should be looking for and should be concerned about, and also timing is a key aspect because we don't want peanut allergic patients to worry about a runny nose in the spring that happens eight hours after exposure, in that scenario they probably have springtime allergies, not their peanut allergy allergic reaction. And so being well educated about timing and types of symptoms can help peanut allergic patients more easily navigate their lives and contextualize when they should worry more.

Dr. Stukus: Okay. So this is fantastic background and I'd like to shift the conversation but I just want to summarize and let me know if I miss the mark here but I'm hearing you describe one, a burden of living with peanut allergy, two, a highly individualized and nuanced approach to sort of management and three, a key component of education of patients and families, do you think that those are all sort of-- is that an accurate sort of summary of what you've described so far?

Dr. Wang: Yeah, absolutely.

Dr. Stukus: Okay. Well with that let's shift gears and let's talk about the buzz worth topic of oral immunotherapy. Help us understand, what kind of treatment does oral immunotherapy offer for peanut allergy and the question everyone wants to know is is this a cure?

Dr. Wang: The field of food allergy is very excited right now because oral immunotherapy appears to be on the verge of FDA approval for one pharmaceutical product. So what oral immunotherapy entails is exposing the allergic individual to small increasing amounts of peanuts under close medical supervision to try to basically teach the immune system to be less reactive to the allergen. And this approach is analogous to what we already do in the allergy fields for venom allergies and environmental allergies where we're effectively giving allergy shots to teach the immune system to not be so reactive to the tree pollens or the grass pollens that are out there or to be less reactive if a person gets a wasp sting. What's different is the route of allergen exposure for oral immunotherapy is not via shot but via oral, by mouth. And so this is something that the patient would need to take on a daily basis, we start at very small doses so sub threshold levels and increase it over time like a staircase where we aim for a maintenance dose ranging from one peanut to several peanuts depending on the study that you're looking at. This is not a cure but really a treatment strategy to increase the level of protection to help peanut allergic patients and their families better manage on a day-to-day basis and hopefully relieve some of the burden and worry that surrounds the diagnosis.

Dr. Stukus: And to give us a sense of the doses that we're talking about here, what's the amount of protein in say one peanut kernel?

Dr. Wang: So one peanut would equate to approximately 300 milligrams of peanut protein.

Dr. Stukus: That's not very much at all, is it?

Dr. Wang: No.

Dr. Stukus: No, you mentioned research, if you can, I don't expect you to go through all of the different studies that have been done but if you were able to summarize what some of the research surrounding peanut oral immunotherapy has shown us specifically some of the endpoints and what they've demonstrated, I think this would be wonderful for all of our listeners to hear and then we can talk about major take home points after that.

Dr. Wang: Sure. So there have been a number of studies examining peanut oral immunotherapy in the last decade plus and so in aggregate what these studies show is that many peanut allergic individuals are able to be desensitized to peanuts using this small gradual increasing doses process. Estimates range from about 60 to 80 percent success in terms of the number of individuals who begin the process who can ultimately reach the maintenance dose and from study to study there is some variation in terms of what the maintenance dose chosen is. There are side effects though to this process because we are giving peanut allergic individuals a known allergen, so allergic reactions that range from mild to severe have been reported and these can happen to the majority of individuals who undergo the oral immunotherapy process. Common symptoms include oral symptoms as well as GI symptoms but it's important to understand that severe reactions such as anaphylaxis and the need for epinephrine auto injector is a notable side effect.

Dr. Stukus: And just to clarify for anybody who's listening, should oral immunotherapy to peanut or any other food be done at home without supervision or is this something that really requires a very strict protocol and supervised application?

Dr. Wang: Yeah, that's a great question. So the process of oral immunotherapy does require close supervision by a medical professional. What typically happens is that on the first day to start off the process it's done under medical oversight in a setting that is ready to treat the range of allergic reactions including anaphylaxis. Once a safe dose is started then there is a daily dose that is taken at home so there is a part of this process that is done outside of the medical setting but the expectation is there is close communication with the healthcare provider. Any dose increases though absolutely should be done under a medically observed setting.

Dr. Stukus: And the side effects that you mentioned is that only happening at the very beginning or are people experiencing allergic reactions once they've been taking this on a daily basis for quite some time?

Dr. Wang: So allergic reactions can happen at any time unfortunately, there are symptoms or reactions that can be seen during that climb up the staircase but studies have reported that people can have allergic reactions including anaphylaxis even after reaching a maintenance dose and even after being on that maintenance dose for a period of months or even years. And so that is one important aspect that families need to understand is that they will always need to take certain precautions when they're dosing their oral immunotherapy.

Dr. Stukus: And do they need to continue to have their epinephrine with them even though they're undergoing a desensitization protocol?

Dr. Wang: Yeah, as I mentioned before, this is not a cure so we're not fixing or getting rid of the peanut allergy, we're basically teaching the immune system to be less responsive and so the expectation is that this treatment strategy is in addition to maintaining peanut avoidance meaning reading ingredient labels and clear communication with anyone who prepares food that there should not be peanut intentionally in that dish as well as maintaining an epinephrine auto injector at all times because allergic reactions can happen to the treatment itself, the oral immunotherapy but potentially also outside in a restaurant or such if the threshold of exposure potentially exceeds what level of protection is afforded by the oral immunotherapy.

Dr. Stukus: And going back to some of the research that you mentioned, most of those, are those reported after following patients for say six months, twelve months, are they following for ten years, give us a better sense of how long people are really being followed to see what happens?

Dr. Wang: Yeah so the data out so far is really on the short term range, some studies have been half a year, other studies have been a year to a few years, there's very little data looking at how people are doing five, ten plus years out from immunotherapy because this is a relatively new treatment. And so right now the largest study to date is a phase III study that was published last year by Aimmune showing that there was a success rate that effectively matches what has been seen in other smaller studies and adverse effects rates were also fairly comparable. Right now there is ongoing efforts to follow these patients out longer within that phase III study but also there are other studies looking at long term outcomes of peanut oral immunotherapy so hopefully we'll get a better understanding over time of how people are doing.

Dr. Stukus: And the idea if and when this is put into practice that this is really long term management that's going to last years if not indefinitely, is that correct?

Dr. Wang: Correct, yes, the conversations that we're having now with families is precisely this, that this is a treatment such as what we would see for a diabetic or someone with hypertension is that we start treatment and really expect the treatment to be ongoing indefinitely. Certainly we would hope that at some point in the not too distant future that we'll find a way to actually cure people but oral immunotherapy has not proven to be that yet.

Dr. Stukus: And back to the research, you mentioned a couple of things I want to circle back to, one is that it's not 100 percent successful and a follow up to that is how do these research studies sort of define success, was it participants underwent like an oral challenge at entry and then they were able to tolerate a higher amount at the end of the study or what else did they look at?

Dr. Wang: Yeah, these are great questions and I think they're best illustrated by talking about the phase III study that was published last year, so in that city about 20 percent of participants dropped out so did not complete the protocol and reach maintenance and of those 20 percent, a little bit more than half actually dropped out because they had side effects that the family felt was intolerable or was not worth the efforts to push on in the process. There were others who dropped out for a variety of other reasons because I had mentioned as an example that this require every day dosing and there are some

precautions that we do advise patients to take such as doing a relatively quiet activity for two hours afterwards and not dosing when they're ill and those types of parameters, it's a little hard for some families to find the time to be able to manage the oral immunotherapy process and so a subset of individuals drop out because this process is just not something that fits well with their lifestyle.

Dr. Stukus: And then you were going to talk about the sort of endpoint, was it an increased amount of peanut people could tolerate or what did they actually look at?

Dr. Wang: Right so in this phase III study again similar to some of the other studies that were published, individuals underwent a baseline food challenge to identify the threshold dose of peanut that triggered an allergic reaction and then at the end of treatments, the subjects again underwent another food challenge to see whether that threshold changed or not. The study also examined the severity of symptoms that developed at the different food challenges and compared the two. So the outcomes of success is really defined by the food challenge.

Dr. Stukus: So it looks like right now at least the published research is showing an ability to tolerate higher levels but as you mentioned, you can't just eat as much as you want necessarily.

Dr. Wang: Correct. So again going back to this study as an example, patients who entered this study had to react at less than, at around a third of a peanut whereas at the end of the study they were found to be able to raise the thresholds for two-thirds of them to two peanuts. So for a significant number that threshold did increase very nicely such that we think two peanuts certainly should be enough to protect from the kind of everyday outside accidental exposure to peanut.

Dr. Stukus: The trace amounts and cross contact that you were talking about earlier, is that what you're referencing?

Dr. Wang: Correct.

Dr. Stukus: Oh got you.

Dr. Wang: Correct yeah, so the expectation is not that these people will be making themselves peanut butter sandwiches or ordering peanut butter cookies outside, they would still maintain their usual avoidance strategies but this provides a buffer such that in case some mistake is made anywhere along that path of acquiring the food, preparation, et cetera to the person consuming it that if some mistake happened along that process that the individual will be less likely to have an allergic reaction and/or if there is an allergic reaction the symptoms would hopefully be milder than what it would have been had they not undergone the oral immunotherapy process.

Dr. Stukus: Okay, that's a great summary. And so I'm hearing you describe that this it's a build up period with pretty regular visits to the physician office to actually receive the next higher dose then it's taking this every day for a prolonged period of time, you mentioned some of the risks involved in regards to side effects. I'd like to hear your thoughts on the benefits, why pursue this in the first place?

Dr. Wang: Yeah so as I mentioned before, the burden on a daily life for peanut allergic individuals is quite high because they have to constantly be on alert and basically worry that even if they do everything right meaning that they read the ingredient labels or they communicate to the waiter or the food preparer that everybody understands clearly and takes the precautions necessary to ensure safety of that food product because we know that mistakes do happen and that's been reported in the literature that peanut allergic individuals, despite the best of intentions, allergic reactions do happen, this oral immunotherapy process by raising the threshold that was to trigger an allergic reaction hopefully will provide families with potentially the peace of mind that if some mistake happens that their child or themselves would be less likely to have an allergic reaction or as I mentioned certainly a milder reaction than what would have been had this process not been started.

Dr. Stukus: Yeah so as you mentioned for those families that have a lot of anxiety surrounding this or those that are exquisitely sensitive are given that buffer, it sounds like a good benefit.

Dr. Wang: Yeah, and up until now the management strategy really relied on strict avoidance of the allergen and this preparedness with epinephrine auto injector and to some families that felt like a very passive approach, they almost have to kind of wait and see and if they have a reaction they'll deal with it, if they don't then phew, great. Whereas with this process I think a lot of families feel that they can have a more proactive approach to gain that buffer that hopefully will improve their day-to-day functioning.

Dr. Stukus: Implementation is always the tricky part, right, everything kind of sounds good on the surface but then really thinking through the nitty-gritty details is where we sometimes find that challenges occur. What about on the allergist end, what do allergists who offer oral immunotherapy need to consider in regards to implementing this with their office setting?

Dr. Wang: Yeah, that's a great question and I think us allergists are very excited that we potentially have something new to offer our patients but it is practice impacting, with the number of visits that each individual will need to have, that will increase the workflow for us in terms of physical space to be able to see all of these patients, appointment slots, et cetera. We also know that this process, there's a huge learning curve for the doctors, their practice staff as well as the families and so at the beginning there often are a lot of phone calls that come through to us asking questions about, "Is it okay to dose because my child had the sniffles?" or, "Oh this came up and we don't have the two hour window to do a quiet activity, what should we do?" And certainly I mentioned allergic reactions to the doses, families will contact us to better understand how to manage and whether to change your-- change in doses would be needed, et cetera. So this is something that for any allergist who is considering or already does requires a thoughtful process in terms of how to incorporate patients undergoing oral immunotherapy into a busy practice.

Dr. Stukus: And what about from the family aspect, you mentioned not everybody's able to necessarily achieve the maintenance dose for a variety of reasons, so do we know sort of who's the best candidate to undergo peanut oral immunotherapy and are there specifically any risk factors that would make somebody a suboptimal candidate?

Dr. Wang: Right. So as in anything in medicine we always have to get a good understanding of our patients and not every therapy will work for every patient, so some of the things that we really consider at the beginning is one, we want to make sure that the person in fact has a peanut allergy, I mentioned that 20 percent of individuals can potentially outgrow their peanut allergy naturally and so if there is that potential we certainly don't want a family to embark on a long term treatment strategy that requires a lot of effort both at home and coming to office visits if the child in fact doesn't have the allergy, so that's step number one. We also want to make sure that the patient and the family fully understands the goals and purposes and process of oral immunotherapy. Some do not fully understand the effort that's entailed in terms of frequency of visits and what they would need to do at home and others don't fully understand the risk and benefits that are involved in this process which again is no different from most medical interventions, there's always a potential risk and potential benefit and so we would need to make sure that the balance tips in the benefit range and that outweighs the risks involved. So some things that we would consider would be patient specific so if they have underlying medical issues such as asthma that's not well controlled, if they already have one allergic disorder that's not well controlled, that couldn't does bring up the question of whether they would be more prone to have side effects or allergic reactions to the oral immunotherapy as well as if they were not adhering to their asthma medications for example, that would potentially be a red flag signaling us to wonder whether the family would be able to adhere to all the quote unquote rules that we have related to oral immunotherapy. In addition to the medical aspects of it, we also look at the patient and family characteristics and this can involve the child, are they willing and able to cooperate and communicate how they're feeling because if there are allergic symptoms, you'd want them to tell us quickly so that symptoms can be treated and dose adjusted if needed on a family. And as I mentioned this require adult supervision and so having a family situation where there would be an adult who can supervise the dosing and the quiet time for the two hours afterwards and to bring the child to the doctor's visits, the office visits, those are all factors that we would need to consider before embarking on this oral immunotherapy process.

Dr. Stukus: It's a lot to think through and as you discuss all of these different challenges it brings to mind the lessons we've learned in regards to non adherence with asthma management because they're very similar, it requires the daily management plan as well as self management for whenever symptoms occur. And as you know and our listeners do as well, there are so many factors involved as to why non adherence can factor into that and I think hopefully we can extrapolate lessons learned from asthma for oral immunotherapy as well.

Dr. Wang: Yeah, absolutely.

Dr. Stukus: So as we kind of wrap up here this great discussion let's talk about sort of a timely event that occurred and on September 13th, 2019, the Food and Drug Administration convened a panel to discuss the first peanut oral immunotherapy product to be considered for FDA approval which was named AR101 during the research trials that you discussed and will now be called Palforzia. Can you tell us what happened at this meeting?

Dr. Wang: Yeah so that was a convening of an expert advisory panel where they held an open session to really discuss the relevant data surrounding this product looking at both the efficacy data as well as the

safety data and ultimately the panel made the recommendation that the FDA should approve this new drug. Now that does not mean the FDA in fact will, my understanding is often the FDA does align with what the expert committee recommends but that will not happen until the beginning of 2020, so as of now it is not FDA approved, this was an expert advisory panel that reviewed the existing data and made their expert recommendation.

Dr. Stukus: And this drug Palforzia is it actually a medicine or what's actually in it?

Dr. Wang: Yes, so Palforzia is a pharmaceutical grade premeasured peanut flour and so it is food but is being viewed as a biologic because it is manufactured to ensure consistency in protein content from lot to lot, capsule to capsule, so it is pharmaceutical grade but it is peanut flour.

Dr. Stukus: And what's the difference between this Palforzia product that's being considered for FDA approval versus somebody in practice, in clinical practice just using peanut flour to deliver peanut oral immunotherapy?

Dr. Wang: So the difference is that this Palforzia is made in a way to ensure that there is the exact protein content in each capsule as stated on the label, whereas the peanut flour that is used by some in practice there may be some variation in terms of measurements or even batch to batch or lot to lot in terms of how much peanut protein is in a certain amount of peanut flour.

Dr. Stukus: So the quantity may differ because of just regulatory practices as such however it's really the same protein, is that correct?

Dr. Wang: Correct.

Dr. Stukus: Okay. Do we have a sense of Palforzia may cost and as a follow-up does the FDA approval if and when it comes offer any changes in regards to how insurance companies or coverage of this treatment may change?

Dr. Wang: Those are great questions that we don't truly have the answer to right now, the company has not stated as far as I understand pricing amounts but it could be in the thousands range. What would be helpful if the FDA approves it is that it would lead to the establishment of insurance codes to allow for insurance coverage hopefully and this potentially would translate to facilitating OIT moving to a wider clinical practice and thus expanding access to patients.

Dr. Stukus: So this is a monumental event for many reasons, not only because it sort of summarizes our approaches to therapy and that we haven't really had anything for a long time and as you mentioned it really can change the way that we deliver oral immunotherapy across the board.

Dr. Wang: Oh absolutely, this is a very exciting time in the food allergy field, up until now we've had no FDA approved product and it sounds like we're within months from that and I see this really as a first step to potentially more and more treatment options for our food allergic patients.

Dr. Stukus: That's great. Well thank you so much for being with us today and walking us through really all the great background information and summarizing sort of the research to date that got us to where we are today and hopefully we'll have you back on in the future when we have even more data and long term experience with this. And before we say goodbye, is there anything else you'd like to add?

Dr. Wang: Yes actually. Part of the excitements that I have with this in the food allergy world is that while oral immunotherapy we've heard a lot about it and are very excited to look forward to potential FDA approval, there is actually a very robust pipeline of other treatment approaches that are currently under investigation and these include other forms of immunotherapy such as sublingual epicutaneous, but also biologics and vaccines are being explored so we hope as a field that we're actually going to be able to offer our patients several treatment options in the near hopefully not too distant future so that we ultimately would be able to tailor treatment according to individual allergy characteristics as well as patient and family preferences and goals. So I think this is just the tip of the iceberg, we're going to have a lot of different things that we should be able to offer food allergic individuals over time. And I guess the only other thing, the one other thing that I want to mention is that avoidance has been a very successful strategy for many over the years and so for some families, they may choose to continue avoidance as their preferred strategy and it's important I think to remember that this should still remain a treatment option for families which is completely viable.

Dr. Stukus: Oh that's well stated and just to recap again because you mentioned this so many times, as we've heard from Dr. Wang here during our episode, the management of peanut allergy and food allergy is not one size fits all, it's a nuanced condition, it's individualized in regards to the approach to management and now treatment as well. Well Dr. Wang, thank you again for joining us.

Dr. Wang: Thank you, it was my pleasure.

Dr. Stukus: We hope you enjoyed listening to today's episode. Information about credit claiming for this and other episodes can be found at https://education.aaaai.org/podcasts/podcasts. Credit claiming will be available for one year from the episode's original release date. Please visit http://www.AAAAI.org for show notes and any pertinent links from today's conversation. If you like the show please take a moment to subscribe to our podcast through iTune, Spotify or Google Play so you can receive new episodes in the future. Thank you again for listening.