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Preventing Allergic Reactions to Peanuts with a Cancer Drug

**Dr. Turck:**
Welcome to *Clinician's Roundtable* on ReachMD. I'm your host Dr. Charles Turck, and today I'm speaking with Dr. Melanie Dispenza, who is an Assistant Professor of Medicine at Johns Hopkins University School of Medicine. We'll be discussing her research on a cancer drug that may prevent allergic reactions to peanuts.

Dr. Dispenza, thanks for joining us today.

**Dr. Dispenza:**
Thank you so much for having me.

**Dr. Turck:**
Well, to get us started, Dr. Dispenza, would you tell us what prompted you to study acalabrutinib to prevent allergic reactions?

**Dr. Dispenza:**
Well, this is a project that has been over a decade in the making. Let me lay the groundwork a little bit by talking about what actually causes an allergic reaction and why we're using acalabrutinib to stop them. So allergies are caused by the immune system making IgE to substances like foods or pollens, and when you are exposed to your allergen, that allergen binds to its IgE on the surface of mast cells and basophils, causing them to activate, degranulate, and release all those things like histamine that cause symptoms.

So many years ago my colleagues at Johns Hopkins tried targeting specific kinases in the IgE pathway and found that inhibitors of these kinases can help prevent signaling, and therefore, prevent activation of mast cells and basophils by allergens. Unfortunately, many of these kinase inhibitors, the very early versions, were not very selective and were therefore, too toxic for clinical use, but luckily for us, about 10 years ago the first BTK inhibitor, ibrutinib, or Bruton's tyrosine kinase inhibitor, was in development for treating B cell malignancies, and the clinical profile was generally well tolerated in patients.

Now Bruton's tyrosine kinase is one of those essential kinases downstream of the IgE receptor, so my lab and other labs together thought that maybe by inhibiting Bruton's tyrosine kinase we could inhibit any IgE-mediated activation of mast cells and basophils. So we did a lot of early work showing that this works very well in vitro in human mast cells and basophils, and acalabrutinib given to humanized mice that have human mast cells and human basophils in circulation can prevent systemic anaphylaxis to allergens.

So the next phase was to take this into humans and actually see if a BTK inhibitor could prevent a systemic allergic reaction in humans. So our goal was to complete a proof of concept trial, and at the time, the best BTK inhibitor that was FDA-approved was acalabrutinib, which is a second-generation BTK inhibitor approved for the treatment of CLL and other B cell malignancies.

**Dr. Turck:**
So you've talked a little bit about the objectives of your study. Which patients did you include?

**Dr. Dispenza:**
Well, again, this was more proof of concept, and we really wanted to show that this could work for any allergen. In theory, this could work for a food allergy, a drug allergy, or honeybee allergy, but we chose peanut-allergic patients because well one, they're easy to find. There are a lot of peanut allergies out there. But more than that, food allergy trials have a strong precedent for doing what we call food challenges, which is a very controlled procedure that will determine how much food a patient can eat before they have an allergic reaction. And so we chose peanut-allergic patients to include to see if we could, with acalabrutinib, shift their tolerance or the dose of peanut that they could eat before they reacted.

**Dr. Turck:**
And what else can you tell us about the study design and the kind of testing that you did of patients at baseline?

**Dr. Dispenza:**
So when we enrolled patients, we did a baseline oral challenge to peanut. And for anyone who is not familiar with an oral challenge, what this entails is feeding a patient their allergen or potential allergen in incremental doses over a period of time. You start at very tiny doses. In our case we started at, for example, one milligram of peanut. The patient eats it, we monitor them and their vital signs, and then every 15 minutes we slowly increase the dose. As soon as the patient has an objective clinical reaction, we stop the challenge, and we treat them accordingly. And with a baseline food challenge like this, you can determine a patient's tolerated dose of peanut. So we did those at baseline along with skin testing to dilutions of peanut extract, as well as basophil activation testing where we would activate basophils in their blood samples with dilutions of peanut extract as well.

So after we did the baseline oral food challenge, we let everybody have a six-week rest period to recover. We then gave every patient acalabrutinib for two days, and we used standard FDA-approved dosing for B cell malignancies, which is 100 milligrams orally twice daily. And patients returned on the morning of their fourth dose to repeat a challenge to peanut along with skin testing and basophil activation testing.

**Dr. Turck:**
For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Melanie Dispenza about her research on potentially preventing allergic reactions to peanuts with a medication normally used to treat blood cancers.

So now that we have some background on your study, Dr. Dispenza, what were the key findings?

**Dr. Dispenza:**
So this was a very allergic group of patients. We enrolled 10 patients total, and at baseline, their median tolerated dose of peanut was 29 milligrams of peanut protein, and that's actually about a tenth of a peanut, so they could eat a tenth of a peanut before they had a clinical reaction. During their next food challenge, while they were taking acalabrutinib, seven of the 10 subjects tolerated 4,000 milligrams of peanut protein, which is the equivalent of about 16 to 20 peanuts, depending on their size. Actually, 4,000 milligrams was our maximum allowed dose of peanut in the study protocol, so we don't know what would have happened if we'd gone beyond 4,000 milligrams, but it's generally accepted when you reach that level that you're not going to have a reaction no matter how much you eat.

In line with their increased tolerance to eating peanuts, all of the patients also increased their skin test tolerance in a way. In other words, they had reduced skin test sensitivity to peanut extract, and their basophils as well were completely unreactive to peanut while on acalabrutinib.

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**Dr. Turck:**
Now from your vantage point, where do we go from here? What research in this area would you like to see next?

**Dr. Dispenza:**
I think the possibilities are endless. I think we could really think outside the box on how we could use these drugs to prevent anaphylaxis. One of the things that we've thought as a group that these could be very helpful with would be for drug desensitizations, for example. Right now, if someone is allergic to penicillin but really needs penicillin, you'd have to admit them into an intensive care unit, you'd have to call an allergy consult service, and you'd have to do a long labor-intensive and costly penicillin desensitization in order to get someone the penicillin that they needed. But what if you could use a BTK inhibitor, one or two doses, and just to give the penicillin safely without having to do this costly, labor-intensive desensitization procedure? So scenarios like that I think would really change the landscape of healthcare and how we manage allergies to foods, to drugs, to other substances.

**Dr. Turck:**
Now before we close, Dr. Dispenza, are there any key take-home messages from your study you'd like to leave with our audience today?

**Dr. Dispenza:**
Well, I think I would leave the audience with hope. It has been a really exciting year for food allergy therapeutics. Omalizumab was also

approved for food allergy indication. There are new formulations of epinephrine that are in development, nasal sprays or sublingual. I think the landscape of allergy treatment in the next few years is exciting, and I think that it will change lives, and I think it will save lives, so stay tuned.

**Dr. Turck:**
This has been an excellent discussion on the role of acalabrutinib, a drug we normally use to treat hematologic malignancies, to potentially prevent allergic reactions to peanuts and possibly more in future. And I'd like to thank my guest, Dr. Melanie Dispenza, for joining our discussion today and sharing her research.

Dr. Dispenza, it was a pleasure speaking with you.

**Dr. Dispenza:**
Thank you so much. You as well.

**Dr. Turck:**
I'm Dr. Charles Turck. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.