**Transcript Details**
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/dermconsult/psoriasis-treatment-redefined-exploring-the-impact-of-il-23-inhibitors/15836/

**ReachMD**
www.reachmd.com
info@reachmd.com
(866) 423-7849

Psoriasis Treatment Redefined: Exploring the Impact of IL-23 Inhibitors

**Dr. Chovatiya:**
Welcome to *DermConsult* on ReachMD. I'm Dr. Raj Chovatiya coming to you from Chicago, Illinois. And joining me today to discuss updates on interleukin-23, or IL-23, inhibitors to treat adult patients with moderate to severe psoriasis is Dr. George Han, an Associate Professor in the Department of Dermatology at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell in Uniondale, New York.

Dr. Han, welcome to the program.

**Dr. Han:**
Thank you for having me.

**Dr. Chovatiya:**
Now let's dive right in. Can you tell us about the current state of IL-23 inhibition when we think about moderate to severe plaque psoriasis?

**Dr. Han:**
Sure. I think the discovery of this pathway has really revolutionized the treatment of psoriasis. When you think about that furthest upstream kind of master regulator of psoriasis, this is as about as close as we have to really satisfying that need. Right? You talk to your patients and you say, "Look, the psoriasis is overactivation of your immune system, and of course we have to block that to some degree to bring your immune system back into balance, but what we'd like to do is target it as narrowly as possible leaving the rest of your immune system to do what it needs to do." And I think in IL-23 we really have the best target that we can possibly have in psoriasis in some ways.

There are some caveats, of course, but I think it really goes to show that right now in our psoriasis realm, the IL-23 inhibitors are gaining a lot of traction. They're actually the most recent mechanism in terms of biologics that have come to market, but their popularity really, I think, drives home the point that it's a rational target for psoriasis. Why? Because these medicines are very efficacious and have very favorable safety profiles. They really do accomplish what we need them to do for psoriasis, meaning some of the highest PASI 90 and 100 scores that we have come from IL-23 inhibitors, and they also have long-term durability, so I think on those fronts that this really seems to be a good target. We block all those downstream events like Th17 activation, IL-17, which we have other specific inhibitors of, so I think this pathway has a lot to do with activation of psoriasis.

Now when you think about some of the downsides, potentially the medicines in IL-23 tend to work a little slower than, for example, our IL-17 inhibitors. So I think on those fronts, we maybe have a little more room to grow and a little more nuance in terms of selecting the correct treatment for each patient, but there's no doubt that this really has made a big impact on our psoriasis treatment landscape.

**Dr. Chovatiya:**
So to really actually zero in on some of our options when it comes to IL-23 inhibition, I know that we have a few in the tool chest. There's risankizumab, guselkumab, and tildrakizumab; all great choices for individuals with moderate to severe disease. Could you maybe kind of give me your quick snapshot about how you talk about these with your patients and maybe share some of the newer data that has come out in the last couple years?

**Dr. Han:**
Yeah. All these medicines I think in general are highly effective medications for treating psoriasis. You know, we're lucky to be in a

place I think that when you look at most of our newer biologics, the mean PASI improvement is above 90 percent. So when you look at that, it actually really helps our conversation with patients because you know, they always ask you, "What can I expect?" If you tell them, "I expect over 90 percent of your psoriasis to go away," "By the way, we're only going to inject you every two or three months and the rest of the time you just kind of live a different quality of life than you have had," that's actually really compelling. And then they ask you, "What's the catch?" "What are the side effects?" And you can tell them for the most part that for this class of medicines, the side effect profile is really clean such that all of the different percentages for the most part are between 1 and 2 percent of placebo.

You know, there have been multiple studies looking at comparators. I think for the most part, when you look at biologic versus biologic, it's nothing that's too surprising. The IL-17 inhibitors, for example, generally are faster at getting to their outcome measures, but the IL-23 inhibitors do catch up, and it's a difference of a few weeks. It's less than a month, so it's not something that I think is really kind of a total game-changer, but that is one benefit of the IL-17 class. And the other thing is that there has been a recent study looking at risankizumab versus oral apremilast, and to nobody's surprise, risankizumab vastly outperformed apremilast, and especially because they set the targets high at PASI 90. And we know that by looking at apremilast with the PASI 75s are in the 30 percent range. The PASI 90 was really low for this, around 5 percent, and for risankizumab, at week 16 it was above 50 percent, so really no surprise there that it's much more effective at treating psoriasis.

And I always think like if you gave a person the choice of having a medicine that they take by mouth twice a day and by the way has a notable list of side effects that you may very well experience in your first month of treatment versus a medicine that you inject at maintenance every three months, I think the decision paints a different picture in people's minds versus just saying, you know, "Do you want a pill or a shot?"

**Dr. Chovatiya:**
For those of you that are just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Raj Chovatiya, and I'm speaking with Dr. George Han about IL-23 inhibitors for treating adult patients with moderate to severe psoriasis.

So let's switch gears for a moment to the FRONTIER 1 study, Dr. Han. There seemed to be some very interesting positive results coming from this trial, and for those listeners that might not be familiar with it, it's actually looking at an oral blocker of IL-23. So how could the approval of the first oral anti-IL-23 medication change our treatment landscape and discussion when it comes to our patients?

**Dr. Han:**
Yeah. This is really interesting because it really changes our paradigm of how we think about treatments for psoriasis. The reason that we need to have biologics is because that has been our mechanism to provide very specific and targeted inhibition of these cytokines in the past, right? What the antibody drugs do for us is they allow us to design something that very specifically and avidly binds to something else and target it without having many off-target effects. And that's one of the issues potentially with small molecules is that because they're smaller molecules in general, there's more things that they can attach to, and so there's potentially more off-target effects, but there's this whole new idea that maybe through designing a better small molecule you can drive more selectivity but also this idea of constrained peptides.

So I want to talk a little bit about this. So peptide drugs have been around for decades, so it's actually an old technology when you think about it, and all it is is essentially it bridges that gap between antibody drugs and small molecules in that they're about anywhere from about, I would say, 2 to 10 times the size of a small molecule, but they're big enough that they can more specifically bind to a specific area of like, let's say, a cytokine you're targeting; but they're small enough that they can actually be taken orally, and you have enough systemic uptake to actually have targeted effects, so I think that's the big idea here. If you want to boil it down to like kind of an oversimplification, it's an oral version of a biologic—because what is the benefit of biologic? It's really specific targeting and what can these peptide drugs do while it's specific targeting.

So just with that in mind, the idea here is that when you take this oral peptide drug orally, you're able to drive IL-23 inhibition to maybe similar or levels approaching that of a biologic, and I think that's where the FRONTIER trial was really exciting because we're starting to see these high response rates that we really have not seen with any oral molecule. We have some good ones now in our arsenal, but we're really not approaching these levels. And with a grain of salt because it's a phase 2b trial, but you look at the response rates, it's really exciting. We're getting close to 80 percent on a PASI 75 response, around 60 percent for a PASI 90 response, and over 40 percent PASI 100 response rates.

**Dr. Chovatiya:**
And when you kind of keep all this information in mind, Dr. Han, maybe I can pick your brain for a second; how do you think we're going to be having that discussion with our patients about choosing the best treatment option for them? Is it going to be a one-size-fits-all given the general homogeneity of disease? Is there going to be some more nuance to this discussion given the number of treatments?

What are your thoughts?

**Dr. Han:**
I think definitely there's a lot of nuance to our discussions now, and it's getting to the point where it's not only just looking at these outcome measures, which are important, but we're starting to think and talk more about things like molecule size—right?—which, you know, you haven't really thought about. Even though we've had a couple of different technologies with our biologics, including fragments and PEGylation, things like that, it's not something that has been at the forefront of conversation, but we're starting to see not only in the psoriasis space and psoriatic arthritis and hidradenitis, we're talking more about sizes of even different biologics, like some of them are one-tenth the size of the others and what does that buy you in terms of tissue penetration. So I think that's another interesting thing to keep in mind about these smaller molecules like the peptide drugs and small molecules is that you could, potentially, actually have more penetration of these medications into diseased tissue. And so there the idea becomes, do we see any additional benefit in things like psoriatic arthritis or palmoplantar psoriasis? So I think there's really a lot that this opens up in terms of like new avenues of conversation. So unfortunately, I don't think it's going to become easier to have this discussion, but I think as we kind of figure out where these medications kind of have a role in our arsenal, it's just better for everybody because what we want to do is just treat patients, get them to clearer skin, better joints, and better overall health.

**Dr. Chovatiya:**
With that in mind, I really want to thank my guest, Dr. George Han, for sharing his insights on interleukin 23 inhibitors. Dr. Han, thanks so much for joining me today.

**Dr. Han:**
It's been my pleasure. Thank you.

**Dr. Chovatiya:**
For ReachMD, I'm Dr. Raj Chovatiya. To access this episode and others in this series, visit ReachMD.com/DermConsult, where you can Be Part of the Knowledge. Thanks for listening.