Gaps in Research in Psoriasis
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Neil Korman, MD, PhD, interviewed by Brad Glick, DO, MPH, FAAD

BRAD GLICK, DO, MPH, FAAD: Welcome to Dialogues in Dermatology Podcast, March 6th, 2022. I am Dr. Brad Glick and I'm a board certified dermatologist and director of the Dermatology Residency Training Program at Larkin Palm Springs Hospital and Clinical Assistant professor of dermatology at the FIU Herbert Wertheim College of Medicine in Miami, Florida. I will be your host. Today's topic will identify and review gaps in research in psoriasis. Joining me today is Dr. Neil Korman, MD, PhD. Dr. Korman is a professor of dermatology at Case Western Reserve University and senior attending physician at the University Hospitals Cleveland Medical Center in Cleveland, Ohio. He is also the director of the Clinical Trials Unit in Department of Dermatology at UHCMC. In addition, he serves as the clinical director of the Murdough Family Center for Psoriasis, a comprehensive psoriasis research, education and treatment program.

In addition to being board certified in dermatology, Dr. Korman holds subspecialty board certification in dermatologic immunology diagnostic and laboratory immunology. He is a member of the American Dermatologic Association, a psoriasis expert research group, member of the American Academy of Dermatology and Emeritus member of the Medical Advisory Board of the National Psoriasis Foundation and a member of the International Pemphigus and Pemphigoid Foundation Medical Board. Dr. Korman has published over 200 articles in the peer reviewed literature, and since 1997, he has been the principal or co-principal investigator in more than 100 clinical trials, the majority of which have involved psoriasis, including trials of all the major biologic agents approved for psoriasis. Neil, welcome. Thanks for joining us on Dialogues.

NEIL KORMAN, MD, PHD: Thank you for having me. Pleasure to be here.

BRAD GLICK, DO, MPH, FAAD: So let's jump right in. We're talking about gaps in research in psoriasis and maybe gaps in general. Where do we look to identify gaps in our evaluation, workup and management of psoriasis and let's say psoriatic disease? Where do we go for that?

NEIL KORMAN, MD, PHD: Well, fortunately, psoriasis is an important enough disease in dermatology that over the years we've devoted a lot of time in the arena of getting expert opinion. So about, I don't know, it's pushing 15 years ago now, I think the first set of guidelines started to come out about how to take care of patients with psoriasis and there were a series of, I believe six articles, if I'm not mistaken, that addressed what was the disease or what were the comorbidities or what were the drugs and how did you take care of a patient. And that stuff was very important.

And then about five years ago, everybody said the world has changed a lot. We had a many, many new drugs in that period of time. So it was time for a new set of guidelines, updated guidelines, and I have to say the second set of guidelines were dramatically better than the first. The first felt like at times that we were quoting the package insert and there wasn't a lot of interpretation of what the data was, whereas the second set of guidelines was so much better in that regard and so much more explicit about what to do if only people would read them.

BRAD GLICK, DO, MPH, FAAD: It's interesting to me because in hearing you say this and remembering we were waiting for those guidelines forever. I think the last guidelines were Alan Menter and others led that again this time as well, people like yourself involved in the guidelines over the years, but I agree completely. They made them more real world and practical as well. And then really put it together with all of the new, we have topical therapies. There are even some topical therapies that have come to market recently that have not even been part of these guidelines, but I really think they made it more modern day, more real world and more practical. Speaking of the guidelines, which you highlight, and we have those starting back in 2019 and

then another series in 2020, and really a nice update for what we have in our toolbox and also how we look at psoriasis patients.

So we've had a lot of scientific study in bench and clinical trial research, which is identified and included in the guidelines themselves. But in your opinion, what impact has these guidelines had? Have they unmasked more gaps? Did they fill some of the gaps? What impact have they had on our management of psoriasis patients and individual with psoriatic disease in general? And maybe even dig a little bit deeper as to maybe what gaps there still are and have they been filled and if not how we fill them. I know that's a lot of questions right there.

NEIL KORMAN, MD, PHD: [inaudible 00:05:02] All good questions. I'm ready for you. Bring it on, baby. Let me talk first about what you asked about last. Are there still any gaps left? And the answer is absolutely. There's many gaps. Almost all of the studies that have been out there except for maybe a brand new one that has just was approved, I don't know in the last six months or so have looked at chronic plaque psoriasis. And so we don't have data on of guttate psoriasis. We don't have data on palms and soles. And so clinical trials devoted to these specific areas. So to palmoplantar disease, there is a little bit of data there. Some of the biologic companies have had some data there specifically to full on studies for palmoplantar disease, not just a study where the patient had bad psoriasis all over and they happened to have palmoplantar disease.

There's not a whole lot of data on the elderly. There's not hardly any data on pregnant patients. There's not a whole lot of data on people of color. That's it. HIV patients, that's several subgroups where there's gaps or patients who have history of malignancy or patients who have are chronic immunosuppression. There's tiny, tiny little inklings of data on some of these things. And I don't know that we're ever going to get the level of data that we need for. There's not

going to be devoted clinical trials for many of those subsets, but we're going to learn more in the trenches as you call a day-to-day use, maybe some series patient, series of patients.

So you have a case report and then you have a case series, and then you have a small clinical trial, and then you have a large randomized controlled phase three clinical trial that's for registration to get a drug approved. Right. So those are the different levels of evidence. So I doubt we're getting to either of the last two, but we'll get at least hopefully to case series of good numbers of patients for some of those subgroups. All right. So help me with the first questions that you were asking.

BRAD GLICK, DO, MPH, FAAD: Well, one of the things is just kind of a follow up comment and more of an observation to your comments, which is so apropos, and that is there's very few dedicated studies. Now I can think of Secukinumab, for instance, one of the biologic therapy, they did a US scalp study and there have been some other small ones. In fact, same drug, they did a nail study, did a palmoplantar. But to your point, we don't have this detailed data that is specific for those difficult to treat areas, for instance. And we'll usually get that classical post hoc analysis, which is just that bigger group, and then they extract out those individuals. But I don't know how realistically practical that is because it doesn't focus on the specific disease. And I would take it even one step further while guttate psoriasis perhaps is a different animal as it relates to generalized plaque psoriasis. To your point, we really don't have any data on that.

We hear the same things over and over again, group A beta hemalytic strep, some other viral condition may set it off, but nevertheless, there's not really been a lot of specific study. Do you feel that in your clinical practice, do you look to guidelines to kind of determine some of your treatment selection as it might relate to what we've learned in the guidelines regarding therapies or perhaps even comorbidities? And that'll segue into our next question.

NEIL KORMAN, MD, PHD: Yeah, absolutely. I do. I mean, as you alluded to, I was involved in the guidelines, but I'm getting old, so I don't remember what's written always. So I go back and I look at it and see what's there. Even at times when I wrote it, I'm still like, yeah, okay, let me see. Wait a minute, wait a minute. Where is this paper? Let me take a look. So yeah, I definitely do look to the guidelines to help me make decisions in particular clinical scenarios. When I'm in clinic with my residents, they're looking at me, they say, so what's the answer, Dr. Korman? And I say, why don't you go look it up and then we'll talk about it afterwards. Good learning experience, right?

BRAD GLICK, DO, MPH, FAAD: So are there gaps in our understanding of comorbidities? What is the significance of such? What are the role of comorbidities when we're making our therapeutic selections?

NEIL KORMAN, MD, PHD: Well, I think comorbidities are critical, simple kinds of things like, well, generally speaking, you don't want to put a patient on a TNF inhibitor if they have severe heart disease or they have multiple sclerosis and you don't want to put a patient on an IL-17 inhibitor if they have inflammatory bowel disease, Crohn's or ulcerative colitis. So generally speaking, that's the simplistic answer of how you think about comorbidities and treatment guidance, but it's much broader than that. It's like, okay, so you see this patient and they have severe psoriasis and they have severe psoriatic arthritis and well, they had a heart attack and get them to the cardiologist. Okay. I mean, that's the way I think about comorbidities. If they haven't already been to the right specialist, it's time to get them to the right specialist and they're 100 pounds overweight and all the various things, and there's so many new things happening.

You got to pay attention. All the action with the, oh, I just blanked on the class, but the drugs now that are the anti-obesity drugs, the diabetes drugs that at low doses are used for diabetes and at higher doses are now being used off-label to treat obesity and have a 20% weight loss of

body. I mean, it's amazing. These drugs are absolutely amazing, and I think they're critical for our patients with psoriasis. We need to be aware of them. We still need to teach these patients that, guess what? You need to eat less. Guess what? You need to move. Guess what? You need to get a program. And the answer is not located only in a drug, but it's maybe a one two punch for some of our peeps.

BRAD GLICK, DO, MPH, FAAD: Yeah, I'm hearing collaborative care and the collaborative care is not only inclusive of our colleagues, like get me to a cardiologist right away, like you're saying, but it's really collaborative co-management or multidisciplinary approach. I think of emerging comorbidities as a follow-up to the classical comorbidities you allude to, psoriatic arthritis our rheumatology partners, IBD important in the background, but I think we've even expanded that a little bit too. People with uveal disease and psoriatic disease, I think we have to partner up with our ophthalmology colleagues here and there as well too. Even pulmonary, I find myself seeing more chronic obstructive pulmonary disease, a lot more chronic kidney disease in our psoriasis patients. And so I mean, I think for me, to your point, we have to look at the whole patient and I think the cardiovascular story, one that our colleague Joel Gelfand talks a lot about cardiovascular disease and psoriasis, comorbidities, just crucial that we get these patients well, and to your point as well, Neil, it's not just about that drug.

It's not all about that drug, it's about that collaborative care. I want to shift gears a little bit and as we close, maybe talk a little bit about your perspective on where we are now. And I'm kind of thinking therapeutically. We talked about gaps in research, so we did such a great job on that, but where are we now, perhaps in our therapeutic armamentarium, what we've had that's a little bit older that maybe we don't use as much where we are with our current systemic therapies. Maybe make a couple of comments about your approach and maybe even collaborative therapies like combining biologics with other agents or combining biologics with even topicals, which of course we do all the time, but there's new things in the toolbox. So another Glick

question, Dr. Korman. There you go. I've got seven questions in one. Let's see if you can tackle that one.

NEIL KORMAN, MD, PHD: You Glicked me.

BRAD GLICK, DO, MPH, FAAD: I did.

NEIL KORMAN, MD, PHD: It's a verb now, it's a verb now. Okay. So yeah, collaborative care. I totally agree with you. And there's many other specialties. The hepatologist, I used to work with them a lot more when I was using more methotrexate, but I still work with them now when the person's way overweight and low and behold, I've looked at their liver functions or they got hepatitis, little things like that, and I need hepatology involved.

BRAD GLICK, DO, MPH, FAAD: I think that what's important as we close here is to kind of look at where we are now therapeutically. How do you see our therapeutic armamentarium? Are there gaps there? We're talking about gaps, but where are we with our therapeutic armamentarium? In my humble view, what we have now compared to even five years ago, let alone 10 years ago, is remarkable. And it's not just all about that biologic. We've got other things too. We've got new oral systemic therapies, or one in particular that's new, two new topical therapies. So give us your perspective on those possibilities, I guess I would ask.

NEIL KORMAN, MD, PHD: Yep, yep. I totally agree that we've come a long way, baby, and I mean we’re at the point now with our best drugs that we get 100% improvement. We get fully clear skin in more than half of the patients. That just blows me away when I think about it from where we were 20 years ago, 10 years ago. You're right. And our ability with these different new topicals to maybe clean up a little bit that's left in the poor person who's only 96% better and not 100% better. I think there's still new drugs being developed, and there's drugs that are on the cusp of getting approved, the biologic drugs, and as you alluded to the new oral, that's very,

very attractive that patients are getting excited about, wow, you mean Dr. Korman, there's an oral drug I can use now that you don't diss, that you'll have nice things to say?

Absolutely, there is one, because before I would just say, don't waste your time on any of the oral drugs. That's basically how I've kind of like in their faces a little bit in that regard. But I think there's always room for more improvement. Right. We haven't cured psoriasis. Right. We're not the infectious disease docs who can cure hepatitis C with just eight weeks of therapy. Right. So I mean, it's not an infectious disease, so it's not a fully analogous, but it would be nice if we can keep getting more improvement and I think maybe we can.

So I'm very, very sanguine and very optimistic about our future and our ability to continue to make strides in taking care of our patients. Collaborative care is key. It's crucial. As I say to my residents, they need to pick up the damn phone and talk to their colleagues, and that's a hard thing to get across to people, but everybody's overwhelmed and they're too busy and it's too much work, and it's the right thing to do. Pick up the phone, talk to them, make a decision together about what you might do that might be a little outside of the box if you need to combine two things that normally maybe nobody has ever studied before, but maybe in that particular patient, it's the right move.

BRAD GLICK, DO, MPH, FAAD: Yeah, that is so well said. And I agree completely, and I think you're speaking my same language. Having residents in the clinic, one of the things that we want to teach them is to pick up the phone to collaborate with our colleagues. I think it's so important. I want to close with kind of a broad question. As we have moved into an era where we can completely clear people's skin, as I recall broadly for etanercept was one of our first key TNF inhibitors. I think we had about a 10% chance of clearing the skin within a year, and now we have interleukin 23 blockers where there's a 50, 60% chance of clearing the skin completely.

What is your perception, again, I'll take this a little step further of where we've come and what do you think about the new technologies? Now we have a new oral agent that is a tyrosine kinase two inhibitor. We have a couple of new topicals. The one is tapinarof, the other one is roflumilast, different mechanism of action. How do you think they fit into your toolbox and have you had the opportunity to use these new agents? And I think we might even just have one more biologic coming to complete this package of 11 or so that we have FDA approved, and I think we can close with that. What are your thoughts on the new agents?

NEIL KORMAN, MD, PHD: Yes, so I'd love the new agents, and I'm using all of them. I'm using both topicals. I'm using the new oral, and I've just started using the new oral recently, so I haven't seen anybody back. So I don't know the answer, but I know how excited people are when we tell them that, well, here's new medicine that's out that I'm very enthusiastic about it. I want to put you on, and it's not a shot. Oh, Dr. Korman, I heard you only prescribe shots. Everybody told me. Well, I used to, but now I got another piece of great therapy in my armamentarium and you seem like the right person for this.

So I think that and the two topicals, I've been thrilled with tapinarof. I haven't used roflumilast as much. I've used more tapinarof, but so I've used all of these and I am excited about all of them, and I'm excited about the other last biologic agent that's like on the cusp of getting approved. We hope. We think, maybe, maybe, maybe. So a lot of good stuff, a lot of action. I mean, you could almost argue they should write another guidelines now with all the stuff that we just got in a very short amount of time. I don't think it'll happen, but I think that it will happen at some point, but it won't happen tomorrow like I just said. Write a new one now.

BRAD GLICK, DO, MPH, FAAD: Yeah, I think the Academy is also looking at trying to do mini guidelines in between. We have these gaps of six or eight or 10 years, and then writing smaller guidelines in between so that we all stay up to date and at least have some of the guidance

based on a lot of the data that is reviewed in order to create those guidelines. Because for all us to sit at the end of the day and read every one of the articles is a big challenge. I have to tell you, Neil, thank you so much for doing this. This has been fabulous. You are great. I appreciate the opportunity to talk to you about psoriasis and some of the gaps in research and talk about comorbidities, and so thank you very much. Appreciate your time.

NEIL KORMAN, MD, PHD: My pleasure. And it was a pleasure talking with you, Brad, because you're so knowledgeable in this field as well. Sometimes these types of interviews are kind of like a one way affair, so this was definitely a give and take, so it made it even more fun.

BRAD GLICK, DO, MPH, FAAD: Well, for our audience, thank you very much. Until the next Dialogues in Dermatology.