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Advocacy and Research

Speaker 1 (00:00):

Every patient deserves to be seen. The Tremfya Guselkumab Photo Library offers hundreds of real patient photos, easily filtered by patient characteristics, disease locations, and severity. Learn more about Tremfya at tremfyahcp.com.

Ranna Jaraha (00:32):

Welcome to the Practical Dermatology Podcast. This month, we have an interview with Dr. Harrison Nguyen, a conversation between Dr. Neal Bhatia and Dr. Mark Lebwohl, and the latest news from around dermatology. Now, here's Practical Dermatology's Jason Mazda.

Jason Mazda (00:45):

I'm Jason Mazda. I'm here with Dr. Harrison Nguyen, who has a new top-line to his bio. Dr. Nguyen, thank you for joining us. I'll let you introduce yourself.

Dr. Harrison Nguyen (00:55):

Yeah. Thanks, Jason, for having me. My name is Harrison Nguyen. I'm a dermatologist and clinical researcher in Houston, Texas. I manage and direct a practice and clinical research center here called Harrison Dermatology and Research Group. But I'm also a clinical assistant professor at the University of Houston College of Medicine, and just received an appointment at my alma mater, the Baylor College of Medicine in the Department of Dermatology. It's been a tremendous honor and look forward to giving back to the institution that really shaped the foundation of my career.

Jason Mazda (01:28):

Well, big congrats on that. What I want to talk to you about today is, we talk a lot about the great therapeutics available for psoriasis now, but there are some barriers as far as getting the most out of these options. I know that you're passionate about taking on two of these barriers in particular, one of them being diversity in clinical trials. What needs to be done to get clinical trials for psoriasis to the point where all patient demographics are getting the most out of the latest advances?

Dr. Harrison Nguyen (01:56):

Yeah. Thanks for bringing that up. This is a really important gap in the field of dermatology, and it applies to psoriasis, but to all our clinical trials and understanding of diseases. It's important for us that when we do clinical trials, that we have appropriate representation of our entire population in these trials. Historically, our trials have had a big under-representation, especially of patients with skin of color.

(02:36):

As you know, as listeners know, skin diseases affect patients of different skin types differently. They manifest differently, they respond differently, they heal differently. It's really important that companies and researchers are mindful of this gap and are proactive to make sure that when we're enrolling and we are designing clinical trials, that we have representation across the spectrum from our patients.

(03:08):

You mentioned a couple recent changes. There has been some regulatory guidance from the FDA historically, at least in the last 5 to 10 years, that clinical trials must enroll more patients of diverse backgrounds. Specifically, patients of Black and Latino origin. But that rule has been lifted in the last year and there's been a lot of changes from a regulatory standpoint from the FDA. One of those that has impacted clinical trials is that there's no longer guidance for enrolling and studying diverse populations. Now the onus is really on us as researchers and on those who sponsor the trials, whether it's the companies, whether it's NIH, to really demand a diverse representation of study subjects.

(04:18):

The goal of the trial is to be able to take an insight or take data points and extrapolate that to our clinical practice to understand how intervention or a medication can impact a population. But if we have a very narrow population, a very narrow study, that data, those results are not broadly applicable. Again, I think one take-home point is that we really need to, the onus is on us, to be able to enroll and study medications across the entire population.

(04:57):

Now, a second thing that I'd like to bring up, and specifically in psoriasis trials, is that historically, the definition of moderate to severe psoriasis has been restricted to a BSA, a body surface area. It's been greater than 10% BSA, what the FDA has called as moderate to severe psoriasis. But what we know is that the impact of psoriasis is far beyond just a BSA number. It can include involvement of high impact site areas or specialty site areas, which include the face, the groin, intertriginous areas, the hands and the feet, the nails. These areas, even if they have a low BSA, they can really tremendously impact the patient. Even beyond that, some of these sites, such as the nails and the scalp, can be harbingers for systemic inflammation. They can be harbingers for the development of psoriatic arthritis. Nail psoriasis, three-times the risk. Scalp psoriasis, four-times the risk of developing psoriatic arthritis. This is really representative of the fact that psoriasis is a systemic inflammatory condition and that we need to be able to have access to systemic treatment beyond just a BSA.

(06:17):

The final point here is that the FDA, because they have restricted the definition of moderate to severe psoriasis as a BSA percentage, when companies have tried to seek approval for patients beyond just a BSA percentage, the FDA has given a lot of pushback. What we know is that biologics, not only are they very effective, but they also have a very favorable safety profile, especially the ones that have come out in the last decade. We really need access for our patients across the spectrum to systemic treatments beyond just a BSA percentage for our patients.

Jason Mazda (06:57):

OK. That gets into the next one that I wanted to ask you about. When we're talking about prior auths being a big barrier, like you're talking about exactly, I know you've talked about advocacy. What can some of our listeners out there maybe do to affect change as far as legislative action to make some of these systemic therapies, I guess, more readily available to patients who really need them, rather than third-party payers dictating who they're available to and who they're not?

Dr. Harrison Nguyen (07:30):

Yeah, this whole concept of prior authorization, it's reflective of the growing administrative burden on clinicians and on practices for providing access to treatments for our patients.

(07:47):

Before we discuss some things that clinicians can do, I'd just like to touch upon the concept of a formulary, the concept of prior authorization. And remind the audience that formularies and prior auths or not necessarily designed based on clinical data. They're not necessarily designed based on safety and efficacy. But often, they're designed based on financial considerations such as rebate payments. A PBM or a pharmacy benefit manager designs the formulary on behalf of an insurer and often will provide preferred placement for treatments based on rebates, based on how much they're being paid to place a medication higher on the formulary. As such, they have created hurdles, and steps, and processes for us to go through in order to navigate this process.

(08:48):

I think the truth of the matter is that these processes are put in place to create more hassles in hope of potentially deterring the prescription of a medication that is perhaps not as financially lucrative for these PBMs. Obviously, this could be a discussion that we could talk about for hours on end, but there's tremendous hurdles and problems in the drug pricing supply chain and the burden has been put on us as clinicians. It has been put on patients. And ultimately, it's the patients that suffer.

(09:35):

So advocacy is hugely important. We need to continue to advocate as a field, as dermatology clinicians on behalf of our patients so that legislators can understand the burden that these prior auths and these other steps place on us and on patients. Remember, they're not based in safety and efficacy data, but they're based in financial considerations. Reform is already underway. In the last five years, we've already seen some PBM reform happen at the federal and the state level. I am optimistic that change is happening. But it really started with advocacy. It started with shedding light on this matter. The louder that we continue to be to advocate on behalf of our field and on our patients, the more successful we'll be.

Jason Mazda (10:27):

Very nice. Is it a matter of, contact your representatives, or is there anything else specific that you would suggest that people do?

Dr. Harrison Nguyen (10:35):

Yeah. We all know that there's only so many hours in the day and everyone has varying bandwidth that they can really devote to this matter. I think on a very basic level, making sure that you're part of our societies. The AAD, for example, has a huge arm with advocacy and helping support the initiatives that are important to dermatologists and to patients. But a letter to your representative, a letter to different politicians can be very helpful. Helping donate to organizations like the SkinPAC that advocates on these issues as a whole.

(11:21):

Of course, we have some days that are dedicated that dermatologists can join, where they can join on the Hill on the advocacy day at least once a year, where they can go meet with their state representative and discuss some of these issues. When we talk with politicians, it's been surprising to me perhaps how little they're aware of some of the issues that we go through.

(11:52):

I think sometimes it's easy to feel like as one person we can't make a difference, but realize collectively our voice can really make change. Any help that our listeners can provide, whether it's just supporting the local, state, national professional societies, or getting involved in some of these initiatives are really impactful.

Jason Mazda (12:17):

Excellent. Well, thank you so much for joining us, Dr. Nguyen. I enjoy following your LinkedIn page, listening to you on some other podcasts, reading some of the things that you've done, and the passion that you have about some of these issues. Getting to talk to you about them directly was really a pleasure, so thank you for joining us.

Dr. Harrison Nguyen (12:35):

It's really my pleasure. Thank you so much, Jason. Appreciate you having me on.

Speaker 1 (12:39):

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Ranna Jaraha (13:04):

Next, Dr. Neal Bhatia is joined by Dr. Mark Lebwohl.

Dr. Neal Bhatia (13:07):

Hi. This is Dr. Neal Bhatia. I'm chief medical editor of Practical Dermatology. Welcome to the podcast with one of my mentors, good friends, and titans of this specialty, Dr. Mark Lebwohl. Dr. Lebwohl, as you know, he's Dean of Clinical Research at the Icahn School of Medicine at Mount Sinai in New York City. I don't think there's anything Dr. Lebwohl hasn't done, which is probably a tribute because there's going to be a lot more still.

(13:33):

Mark, thanks for joining us on the podcast today.

Dr. Mark Lebwohl (13:36):

Thanks for having me, Neal. I am honored to be interviewed. You're calling me a titan, but Neal is a superstar of dermatology so I'm

honored to be interviewed by you.

Dr. Neal Bhatia (13:47):

That is definitely high praise. I did get to fill in your shoes. We can start out a little bit of psoriasis and work our way through some topics. I did get to fill in your shoes at a meeting where flight challenges gave me the PowerPoint and I got to talk about some psoriasis updates. It's fortunate because we were doing some of the same trials and we talk about these new molecules all the time. Can you give us the rapid fire of some of the new molecules in motion, especially some of the oral treatments that are coming?

Dr. Mark Lebwohl (14:16):

I will just say it's not the first time you've saved me, Neal. You may not remember, but during COVID, there was a virtual grand rounds I think and the speaker didn't show up, and we had minutes to go. I called you and you gave that lecture with minutes. You are a person who knows immunodermatology. It's not the first time, so thank you.

(14:37):

A number of exciting new orals in dermatology. I would say the one right now that's getting a lot of attention is icotrokinra, which is an oral, IL-23 peptide. I will tell you that I was offered the opportunity to do that trial in phase 2 and I thought, "There's no way this is going to ever work. It's an oral, it's going to get digested just like hamburger is. It'll never reach the target." But sure enough, it was digested, less than 1% got through, but that less than 1% was enough to clear psoriasis. In a phase 2, they're showing more than three-quarters of patients achieving PASI 75, which is dramatic for an oral molecule. It beats everything else we have out there. It's getting a lot of attention. The phase 3 data confirmed phase 2. The 52-week data confirmed that the effect is sustained. I think we have a great new oral coming.

Dr. Neal Bhatia (15:33):

It's interesting because we saw the oral TNF, it almost came and went. We saw some other orals that tried to make a pathway, but it seems like this approach of going after 23 might be the winner.

Dr. Mark Lebwohl (15:46):

Absolutely. I will say there is a new oral TNF as well, which is a receptor blocker also. It's the R-1 receptor of TNF. They only showed brief week 4 results, but it actually was impressive at week 4. That may not be a forgotten field. In addition, there's a suggestion that some of the infections and malignancies that have been related in low frequency to TNF blockers may be related to the TNF R-2 receptor. It's possible that shown the good, quick effect with R-1, that may make it competitive at 12 weeks or 16 weeks. I think there's some promise there.

(16:34):

There's also, you probably know, an IL-17 receptor, which was again tested in early phase trials. It looks like an oral IL-17 will be pursued as well.

Dr. Neal Bhatia (16:45):

That would be great. My concern is that I think the tyrosine kinase inhibitors, all the three, one on the market and two coming, they may find their home more with lupus than they will psoriasis because that data is actually pretty striking.

Dr. Mark Lebwohl (16:58):

Their data on psoriasis is among the best data, and lupus is among the best data we have. They may yet have a role in psoriasis. I don't know why deucravacitinib has not done better. Certainly, I use it. The new orals are much safer than the old ones. Acitretin didn't work that well and caused birth defects. Methotrexate and cyclosporine have a million box warnings that are well-deserved.

(17:30):

Deucravacitinib has been a breakthrough for us. It is certainly more effective than apremilast, for example. It's also more effective than acitretin and it doesn't have any of the box warnings of methotrexate, cyclosporine, or acitretin. It offers a pretty good opportunity for us. Not sure why it hasn't done better in the marketplace. It may simply be timing. I think there is an opportunity for TYK2 inhibitors to succeed in psoriasis. And there's no question that they appear to be breaking ground in lupus and in connective tissue diseases. That may be a real opportunity for them, but I think there's still a good place for them in psoriasis as well.

Dr. Neal Bhatia (18:17):

Yeah. That segues into the next thought about hedgehog inhibitors because that's the same vein and the same frustration we have with our colleagues. Why are we not writing more hedgehog inhibitors? There was a consensus panel you were part of, I've been a part of a few as well. What do we need to do to get our friends into these drugs today? It's really very interesting.

Dr. Mark Lebwohl (18:37):

Yeah. The reason they're not being used is primarily muscle cramps. I think the argument to be made here, and this is the way I use them. First of all, I start everyone on L-carnitine, 1000 to 2000 milligrams daily. That dramatically delays the onset of muscle cramps, which with sonidegib was a couple of months. The muscle cramps, by the way, are much less with sonidegib than vismodegib. We actually have switched all our vismodegib patients to sonidegib for that reason. I should actually say, I've been a consulting for all the psoriasis companies, and also for the makers of sonidegib and vismodegib in the past.

(19:25):

Having said that, you can give the drug, have no side effects for many months, shrink the tumor to almost nothing, and then operate on it. That's what we routinely do here.

Dr. Neal Bhatia (19:37):

Yeah. I think the neoadjuvant approach to all of this has to do be on the forefront. I think we've forgotten about neoadjuvant. Just like oncologists, you shrink the tumor, cut it out, and keep it away. That's the mentality that dermatologists need to think about.

Dr. Mark Lebwohl (19:51):

We started doing this a while back, where we shrink the tumor and then we have patients operate on it. Then what ended up happening, there was some patients who didn't get the side effects or got very minimal side effects. They decided they don't want surgery at all and they just continued on the treatment. They've done incredibly well. There's several ways in which we use it. But I agree with you. The neoadjuvant method, treat first, shrink the tumor, and then operate is a better way to go with these.

Dr. Neal Bhatia (20:20):

Yeah. I think part of the lack of uptake comes back to the fact that neither company that promotes the drugs can talk about L-carnitine or stagger 2 weeks on, 2 weeks off, or managing any of the expected outcomes. That's where some of the frustrations are.

Dr. Mark Lebwohl (20:38):

I think using it neoadjuvant is actually off-label, so they have to rely on us from the podium talking about the best way to use these.

Dr. Neal Bhatia (20:47):

Yeah. No, correct. I want to bridge from skin cancer to what goes before that, which is photoaging and rejuvenation. You've gotten involved with a lot of things on the forefront. There's a new molecule or a new class of targets for aging cells called the GPX4 modulator and it works on many different tissues, and it's making its way into dermatology. Tell us a little bit about this initiative.

Dr. Mark Lebwohl (21:14):

GPX4, I don't have any direct experience with, but they just have treated their first patient in a phase 1 trial. GPX4 modulators have a role in a process called ferroptosis, which is similar to apoptosis, and they induce, in essence, cell death. It turns out senescent cells have a role in stimulating chronic inflammation and fibrosis. Think about all the diseases that we treat where these senescent cells actually have been implicated. Psoriasis, atopic dermatitis, vitiligo, alopecia areata, hidradenitis suppurativa. Connective tissue diseases like scleroderma, fibrosis plays a prominent role in that. Dermatomyositis as well. There is a real place in dermatologic diseases for a molecule that would do that. There was actually just a Nature Neuroscience paper showing a role for senescent cells in chronic neuropathic pain.

(22:21):

The design of the trial is interesting. This has been done before with psoriasis where, instead of doing the phase 1 trial in healthy volunteers, they actually use patients. In this phase 1 trial, Rubedo, who make this GPX4 modulator, are going to be using patients with inflammatory skin diseases like psoriasis and the diseases we just mentioned, and also will study patients with actinic keratoses and otherwise healthy aging skin. The drawback of course, of a phase 1 trial, is you can only treat patients for 1 month so we're not going to get 16-week data. But we will get 1-month data and they're going to look and see. Did we indeed impact senescent cells? Did we reduce senescent cells? I think that there is some real promise there.

Dr. Neal Bhatia (23:19):

They did some work in vitro too, with the biopsy specimens-

Dr. Mark Lebwohl (23:22):

Yes.

Dr. Neal Bhatia (23:23):

Which is great because immune senescence, if we're not modulating how much of the immune system is not doing its surveillance job, we're already going to be behind. That's where I think we do our work. This is real exciting. I think even more so, you think about the future of talking about aging and how can we slow some of that process down, I think this is where the forefront will be, so that's great.

(23:48):

Mark, I really appreciate your insights on all these important topics. Not only what we've done and where we're going, but keeping research alive. I think you and I and a bunch of our other colleagues really want to put our foot on the gas and not on the brake.

Dr. Mark Lebwohl (24:02):

Yeah, yeah. I think a lot of our friends deserve to be patted on the back. The amount of breakthroughs in dermatology over the last two decades has been extraordinary and there's been a real force of dermatologists contributing to that, and you being one of them.

Dr. Neal Bhatia (24:17):

Well, thank you.

Dr. Mark Lebwohl (24:17):

So thank you.

Dr. Neal Bhatia (24:19):

Without innovation we'd be lost, so I think that's good. This was a great episode of our podcast for Practical Dermatology. Dr. Lebwohl, thank you again for taking the with being with me. We'll see everyone next time.

Dr. Mark Lebwohl (24:31):

Alrighty. Take care. Thanks for having me.

Speaker 2 (24:34):

And now for the news. Our top story looks at healthcare disparities affecting patients with atopic dermatitis. New research published in the Journal of Drugs and Dermatology show that patients living in low income counties face higher out-of-pocket costs for atopic dermatitis care than high income counties. The study looked at the comparative costs of commonly purchased skincare items available in major retailers, including Amazon, Walmart, Walgreens, CVS, Target, and Meier. It also specified higher quality products approved by the National Eczema Association, and compare them to non-NEA products.

(25:06):

According to their analysis, higher quality NEA-approved moisturizing lotions and liquid body soaps cost more than twice as much as popularly purchased alternatives. Lower income areas were also more likely to be pharmacy deserts for these patients. They tended to have fewer retail stores per capita, reduced store operating hours, and reduced in-store product stocks. The research team said the findings underscored the urgent need for targeted policy efforts to improve equity in dermatologic care access.

(25:35):

Guselkumab continues to demonstrate its versatility, this time for scalp psoriasis in patients with skin of color. According to new data from the Visible Study first presented at AAD 2024, guselkumab significantly improves scalp psoriasis symptoms across diverse racial and ethnic groups. Nearly 80% of participants in the study reported noticeable scale clearance by week 24. Patients also saw improvements in a number of secondary endpoints, including DLQI and PSSD scores. The authors emphasize the trials diverse cohort. Approximately 50% of participants were non-white, calling it "an important step toward more inclusive dermatologic research."

(26:14):

In the latest edition of Practical Dermatology C-Suite Chats, Haut.AI founder Anastasia Georgievskaya talks about the impact of new artificial intelligence tools, such as a virtual skincare try-on that shows customers how sunscreen and its ingredients will impact skin over time, as well as the changes the technology is bringing to the industry. Here is a portion of the feature.

Anastasia Georgievskaya (26:34):

We already have multiple examples how AI is leveraged at different steps of the product development and marketing. Essentially, AI now shares some of the traits it did for pharma company, and essentially it allows companies to discover new molecules or find the new targets for existing molecules on the market, essentially helping strengthen a key portfolio of the brands. As we know right now, it's extremely hard to launch a brand if you don't have strong IP and proper to the molecule. AI can make your go-to-market play faster, as opposed to not leveraging AI in trying to find your superstar hero molecule.