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Calling Out Hesitation on Systemics

Ranna Jaraha:
Welcome to the Practical Dermatology Podcast from the editors of Practical Dermatology, I'm Ranna Jaraha. In our top story, the FDA has approved Dupixent for the treatment of adults and adolescents aged 12 years and older with chronic spontaneous urticaria. The approval marks the first new FDA-approved therapy for the indication in more than 10 years. According to Regeneron and Sanofi, Dupixent is now approved for the treatment of people aged 12 years and older with CSU whose disease is not adequately controlled with H1 antihistamine treatment. The FDA approval of the blockbuster drug for chronic hives becomes the seventh FDA-approved indication for dupilumab. The approval was supported by data from the multi-study LIBERTY CUPID phase III clinical program. Study C, the second LIBERTY CUPID pivotal study in biologic-naive patients met its primary and key secondary endpoints confirming results seen in the previous Study A. Results showed dupilumab significantly reduced itch and urticaria activity. Safety results in all LIBERTY CUPID phase III studies were generally consistent with the known safety profile of dupilumab and its approved indications.

In a news release, Dr. George Yancopoulos, board co-chair, president, and chief scientific officer at Regeneron stated, "With this FDA decision, Dupixent is now approved for seven chronic debilitating atopic conditions driven in part by underlying type two inflammation, several of which have been shown to co-morbidly occur with CSU such as atopic dermatitis and asthma, providing patients with one treatment that might help multiple atopy conditions. We look forward to bringing Dupixent to the more than 300,000 CSU patients in the US with inadequately controlled disease on standard of care treatment who until now had limited treatment options." Dupixent was first approved in 2017 for atopic dermatitis. Most recently in September it became the first biologic product for chronic obstructive pulmonary disease.

A new study shows that Johnson & Johnson's Icotrokinra, an investigational oral IL-23 receptor antagonist led to completely clear skin in 75% of adolescents with moderate to severe plaque psoriasis by week 24. According to results presented at the 2025 World Congress of Pediatric Dermatology, in a subgroup analysis from the phase III ICONIC-LEAD study, adolescents treated with once-daily Icotrokinra achieved high levels of skin clearance. By week 16, about 84% of adolescent participants achieved an IGA score of zero or one, and 71% achieved a greater than or equal to 90% reduction in PASI 90. The outcomes improved through week 24 with 86.4% achieving IGA 0.1 and 88.6% reaching PASI 90. A total of 75% of adolescents achieved IGA zero and 63.6% achieved PASI 100. For safety, at week 16, half of adolescents on Icotrokinra experienced at least one adverse event compared to 73% in the placebo group with no new safety signals identified. Johnson & Johnson said it is initiating the phase III ICONIC-ASCEND study, the first head-to-head study seeking to demonstrate the superiority of Icotrokinra taken orally compared to an injectable biologic.

This week, Practical Dermatology launched a new series called Updates on Skin Cancer, in which leaders in the dermatologic space provide updates on the latest trends and innovations in the treatment of melanomas and carcinomas. In the first episode, Dr. Hadas Skupsky, a board-certified dermatologist and dermatopathologist, discusses gene expression profiling technology and its importance in the diagnosis and prognostication of melanomas.

Dr. Hadas Skupsky:
When we still have ambiguity despite using IHC, we still have questions. That's when we'll often consider molecular testing. And so from the DNA side we have things like next-gen sequencing, we have comparative genomic hybridization, and we have FISH, fluorescent in situ hybridization. These are all methods that are looking at the DNA. GEP is unique in that it is looking at the RNA, so this is looking at the RNA that's actually transcribed in the tissue at the time you did the biopsy. So it's looking at the RNA that is produced by the tumor and its environment, measuring the expression of specific genes of interest and a proprietary algorithm will look at the amount of the genes that are being expressed, compare that to a widely studied and validated group of lesions that had a known outcome, meaning

they're known melanoma or they're known benign, and able to categorize, give a score and say, "This is more likely to be benign or this is suggestive of malignancy." So it is giving an objective input to weigh in along with all your other inputs.

It's really important to realize that the GEP is not meant to be a be-all end-all answer. It's not meant to replace the pathologist or all the other ancillary tests that you may have done or the clinical information that you have. It's meant to be one additional input that you then integrate with all the other information that you have.

Ranna Jaraha:
For a spotlight on psoriasis, we spoke with Dr. Linda Stein Gold.

Jason Mazda:
I'm Jason Mazda with Practical Dermatology, and I'm joined by Dr. Linda Stein Gold to talk a little bit about psoriasis today. Dr. Stein Gold, with 10 FDA approvals in the past 10 years for psoriasis, how much has the ability to treat that condition evolved?

Dr. Linda Stein Gold:
It has been such an exciting time. I mean, we've seen major advances. And what's exciting is that these advances have not only been in the biologic arena, but we've also seen them in the topical and oral arenas as well. So what this does is it gives us a lot more tools to meet the demands of our patients. We basically have the ability to get a significant number of our patients to clear almost clear skin, and our goal really is to try to have our psoriasis patients live lives that allow them not to think about their psoriasis.

Jason Mazda:
And something you and I talked about a couple of months ago was that when a big piece of research comes out about one particular drug, it's not necessarily a matter of this drug is better than everything else, and this is going to outperform everything and be the number one choice for every single patient. How important is it just to have so many good options? So if one thing doesn't work, to know that something else might work, knowing that a different drug might be best for each different patient?

Dr. Linda Stein Gold:
Yeah, it's so important because we know that even though we have these really wonderful options, no one drug works for every single patient, and we know that each of our patients has unique needs. So we have to have a lot of these tools, we need to have great biologics, we need to have great orals, we need to have great topicals. And by having this array of options, we can really look at the individual needs of our patients and try to give them a life where they don't live their lives around their psoriasis.

Jason Mazda:
Fantastic. Well, thank you so much for joining us today. That was really enlightening. Thank you.

Dr. Linda Stein Gold:
Thank you, Jason.

Rana Jaraha:
For this week's one-on-one, Practical Dermatology chief medical editor, Dr. Neal Bhatia is joined by Dr. Jason Hawkes.

Dr. Neal Bhatia:
Hi, I'm Dr. Neal Bhatia. I'm chief medical editor of Practical Dermatology. I'm here with my good friend, Jason Hawkes. Jason, tell us how you're doing and where you're practicing today.

Dr. Jason Hawkes:
Hi, everyone. Jason Hawkes, medical dermatologist, principal investigator at the Oregon Medical Research Center in Portland, Oregon. And happy to be here today.

Dr. Neal Bhatia:
I say where you're practicing today because I'm happy that you're moved and settled into a great new place, so that's great.

Dr. Jason Hawkes:
Yeah, enjoying the cooler weather than warm California, burning California.

Dr. Neal Bhatia:
Burning California with better taxes than Oregon too. So one of our favorite subjects is calling out dermatologists who say they're not comfortable with systemic therapies. I want to just unload on some of that because I talked to people in high places about JAK inhibitors about shots for psoriasis and atopic dermatitis. I just don't understand what more comfort level do we need when we have so many studies that have five-year data, we see safety signals that are minuscule that pertain to these drugs. Tell me, what's your approach to how to, again, bring someone down off the ledge about writing drugs that actually work?

Dr. Jason Hawkes:
Yeah, I've started having the conversation with both provider and patient about their approach to, "I'm doing well and I don't want to add something in my body which might immunosuppress me or increase my risk for infections." And so the mindset for some of these providers and also patients is that if they do nothing, there's safety. And then if they add something, they might add some level of harm. The myth to that though is that having these diseases alone, inadequately treated, doesn't have its own harm, and that's the flip side of the coin. The counterweight is that inadequately treated psoriasis or widespread eczema has its own negative impact. So I think the comorbidities of psoriasis is probably the best example where we're seeing increased risk of cardiovascular disease, stroke, kidney disease, sleep disorders, mood disorders, substance abuse.

So this idea that if I do nothing, it's safe, and if I add a medication, it's unsafe. We have to start to balance that if you do nothing that has its own impact. And probably some of these comorbidities have a higher health risk or increasing mortality, for example, compared to these theoretical risks with some of these medications. And some of the medications like with the JAK inhibitors, for example, are real. They're just so small. We're talking about sometimes one to two events per 100 patient years. That's a hundred years of continuous treatment. So I just don't think we're having the conversation with patients that creates that balance because when I bring this up, a patient will often say like, "Oh, I had no idea that my bad widespread psoriasis or eczema could have a health impact." So then they feel more motivated to manage it. And I think the providers, if they also kind of saw that concept that we're trying to decrease the systemic inflammation to reduce other health risks, that's really the fair balance playing field.

Dr. Neal Bhatia:
It's interesting. I was at Winter Clinical and I heard Ron Vendor, he is a good friend of mine from Ontario, and he quoted one of the old Rush songs Freewill. And one of the lines is, "If you choose not to decide, you still have made a choice." And that's kind of the mindset that patients are in now. They sit there and they don't want to make a choice about therapy because they think they've heard something, and yet what they're not doing is they're not recognizing the costs and the time that they're losing by not treating themselves. And you think about the psoriasis patient with metabolic syndrome or the atopic patients whose barriers are going down the drain and everything else in between, between sleep and concentration of work. I mean, I just don't, again, follow why do we have to go back to drugs like methotrexate and cyclosporine that are Th1 drugs for a Th2 disease, or when we have to go to a point of putting patients at risk of different toxicities when the disease itself has more toxicity than some of these therapies.

Dr. Jason Hawkes:
Yeah, no, they're good points. I mean, I've always said this, you and I have talked about this where it's not really a safety issue. This is the smokescreen that people use because they're very willing to give two weeks of prednisone, oral prednisone or intramuscular Kenalog or cyclosporine, methotrexate. These are medications with very real reproducible safety signals. At high numbers, prednisone alone, that has huge impacts on the body. And cyclosporine, we know these patients when they're immunosuppressed broadly, there's a whole host of issues. And that's not even talking about some of the secondary end organ issues that we see. So this idea that it's about safety doesn't really work because they're using medications that have very low narrow therapeutic indexes as opposed to these medications, even some of the biologics that really don't. And I think the JAK inhibitors understandably have probably frightened some providers just because of the way that the FDA tackles black box warnings. But it's all about relative safety, the relative safety of the JAK inhibitors to these broad acting immunosuppressants, it's night and day different.

Dr. Neal Bhatia:
Oh, absolutely. I mean, you'll look at anything that we do with a promotional deck, a package insert, anything else that's always littered with safety information that looks like it's nothing but poison rather than actually thinking about outcomes. And just real quick, I mean we talk a lot about five-year data. I mean, why would someone run a five-year study if it weren't to save drug? I mean, that's what is counterintuitive to me. But we talk about five-year data with the JAK inhibitors for atopics. We have tyrosine kinase two inhibitor data for five years. I mean, how do we get that data into the hands of the patients that says, "Look, patients have done well for five years both in trials and in real world." What do you still see here that is an obstacle to getting you in this car today, for example?

Dr. Jason Hawkes:
Yeah. Well, it gets back to the age-old question, which is how much data is enough? So I think there are providers who five years, 10 years, 15 years, it probably isn't really going to change behavior. But I think we haven't really uncovered sort of the truth as to why some providers don't necessarily use these medications. Maybe it's the administrative burden, maybe it's the cost of the loss they have in practices for actually prescribing and having to have staff do PAs. We understand that piece, but dermatologists have always done well, even when we prescribe these medications. And at the end of the day, it's really about the patients and trying to get them to that point. It's very unlikely that we pick up a new signal on year 10, for example, that we didn't pick up at year five.

And I think the five-year data, particularly in the Tyk2 with deucravacitinib, showed basically no new safety signals. And even with

upadacitinib, which has had the longest running data, I think the concern for MACE events and clots and serious infections are much lower than we thought about before. So I'm hoping that as an evidence-based specialty in medicine, that they could take this data and say, "Okay, maybe this allays some of the concerns." If it doesn't, then we say, "Okay, well, what's the real concern?" Maybe it's not really about safety. And my suspicion is that there's still some of those other concerns that aren't really rooted in safety because the data is pretty reassuring for these molecules.

Dr. Neal Bhatia:
No, absolutely. And this is the kind of conversation that I think a lot of our colleagues need to hear as well as a lot of the patients need to hear, so I think that's good. So, Jason, now that you've moved to Oregon, I got to get you out of the habit of seeing providers and seeing clinicians, because in California all they do is provide headache. And in Oregon, they actually are real clinicians who practice medicine.

Dr. Jason Hawkes:
Yeah, that's true. So it's the terminology and hopefully we get to a point where we even have healthcare advocates, the people that are actually advocating for patients to get improving care and better outcomes. And these agents that have come out have done such a good job at clearing disease that we have to start acting in the best interest of our patients as opposed to what maybe helps business. We need to balance those things and keep the patients at the forefront of what we do in the clinic.

Dr. Neal Bhatia:
Oh, absolutely. The nice thing too is in September when the dermatologists go to Capitol Hill, we bring patients and the patient advocacy groups with us, and those voices tend to resonate a lot, so that should be something worthwhile. All right, Dr. Jason Hawkes, always a pleasure, always bringing the wisdom as we try to do. Let's hope it doesn't fall on deaf ears.

Dr. Jason Hawkes:
Yeah, thanks for having me.