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Reviewing New Therapies for Hidradenitis Suppurative

Dr. Chovatiya:
As the pathogenesis of hidradenitis suppurativa, or HS, becomes better understood, the treatments for this condition just seem to be increasing. So what do we need to know about the therapies that are in the pipeline?

Welcome to DermConsult on ReachMD. I'm Dr. Raj Chovatiya. And joining me today to discuss emerging treatment options for patients with hidradenitis suppurativa is the one, the only, Dr. Martina Porter. She's a dermatologist at Beth Israel Deaconess Medical Center, an Assistant Professor of Dermatology at Harvard Medical School, all-around HS expert, and wonderful human being.

Dr. Porter, welcome to the program.

Dr. Porter:
Thanks so much for having me today. Hopefully, I'll have some insightful things to share.

Dr. Chovatiya:
Well, let's dive right in now that I've got you in a good mood. So what new therapies are emerging for the treatment of HS? Million-dollar question here.

Dr. Porter:
Yeah. So I think the million-dollar answer is that they just completed two of the biggest, if not the absolute biggest, trials for IL-17 inhibitors for HS. So one was for secukinumab, which is the IL-17A inhibitor, which they published their both week 16 and week 52 data, and the second was for bimekizumab, and so far they have shared with us the week 16 data but not their data out to week 48. But besides this, we've actually seen a lot of other interesting clinical trials for different molecules—IL-1 inhibitors, JAK inhibitors—which are now entering the phase 3 pipeline, IL-36 inhibitors. I think the list could go on.

Dr. Chovatiya:
That's amazing. I mean, I can even think of a time where if we really looked at clinicaltrials.gov, it seemed like an empty desert, but now you really can't throw a stone a very small distance without hitting at least one of many HS trials, which is exactly what we need. Let's zero in on secukinumab to start with. Can you tell me a little bit more generally about what is its efficacy, its safety, and where it might fit into what we have?

Dr. Porter:
Yeah. So secukinumab, as most people know, is an IL-17 A inhibitor, and we've used this for many years now in psoriasis and for our patients who have psoriatic arthritis, but actually, the phase 3 trial looked at two different doses. Both were loaded with the same secukinumab 300 milligrams every week for the first five weeks, the same as we do in psoriasis. And then they actually had two arms, which was every-two-week or every-four-week maintenance dosing. And I think in terms of the efficacy, the good news is that the drug met its endpoints, and so just under half the patients achieved high score or high score of 50 at 16 weeks. The interesting thing, too, was out to 52 weeks, patients actually continued to improve beyond 16 weeks, and it really looked like the peak was closer to around the six-month mark. So I think one of the things to note when we see this drug become available is it won't really be clear at first what dosing to use because the two- and the four-week dosing actually had about the same results. And then we also I think need to be a little more patient with this drug because after four months it still really hasn't hit its peak.

From a safety perspective, it really is the same essentially. The two- and four-week dose is what we saw and what we know from psoriasis. And even for patients with HS who we know have a higher risk of inflammatory bowel disease, we didn't really see that really emerge from the trials even though patients with IBD who were well-controlled were allowed to enter.

Dr. Chovatiya:
You and I have talked a bit about the availability of TNF inhibitors as a treatment option. It seems like there are some patients it's a better choice, some patients not, and it's really nice to see another drug's different target meeting its endpoint. And hopefully, we're going to learn a little bit more about who might be the right kind of patient for what therapy.

Dr. Porter:
Oh yeah, I agree. And I think for patients having used this drug off label for a number of years now, there's something about knowing the safety profile for many years, even if it wasn't for HS, and also knowing the safety profile is slightly better than the TNF-alpha inhibitors that I think encourages patients, and they're interested in starting biologics like IL-17 inhibitors, even if they weren't that interested in the TNF-alpha inhibitors.

Dr. Chovatiya:
Great point. And that brings me to a newer IL-17 inhibitor, probably the newest one that we'll have in this country though available ex-US for some other indications. Can you tell me a little bit more about bimekizumab—what it is, what it's used for, safety, efficacy, and where you see this all falling out?

Dr. Porter:
Yeah. So bimekizumab is also an IL-17 inhibitor, but it actually targets both IL-17A and F, and there is some thought in the HS world now that IL-17F may be an even greater driving factor in this disease. The data that they published so far is only out to week 16, and it honestly is about the same as what we're seeing for both secukinumab and adalimumab. The difference is all the other trials have used high score 50 as an endpoint, which is just a 50 percent improvement in their abscess and nodule count, but bimekizumab actually showed data for high score 75, so they're raising the efficacy bar now looking at 75 percent improvement in the abscess and nodule count, and they're really seeing that patients are hitting both the 50 and the 75 percent improvement mark, which may be a lot more significant in the long run for some of our patients.

Dr. Chovatiya:
Amazing. And for those of you just tuning in, you're listening to DermConsult on ReachMD. I'm Dr. Raj Chovatiya, and I'm speaking with Dr. Martina Porter about treatment options on the horizon for patients with hidradenitis suppurativa, or HS.

So, Dr. Porter, tell me, are there any JAK inhibitors that we should know about just given that that's pretty much all we've been talking about for the past few years when it comes to dermatologic disease?

Dr. Porter:
Yeah. So JAK inhibitors are also now being studied for HS. Both, upadacitinib and a new drug povorcitinib, which are both essentially mostly selective for JAK1, have finished their phase 2 studies with some promising results as well, so they're both entering phase 3 now. I would say the safety profile is probably getting closer to what we see in the RA trials than what we were seeing in our atopic dermatitis trials because these patients with HS seem to have inflammation that is more similar to RA patients than eczema.

Dr. Chovatiya:
Do you think that there's any relationship, potentially, when thinking about that tradeoff with efficacy and safety to just the underlying risk factors in each individual patient knowing that the comorbidity profile is obviously very different from an HS patient, an IBD patient, an atopic dermatitis patient—or even an alopecia or vitiligo patient?

Dr. Porter:
Essentially, I think both patients and physicians are really focused a lot more on safety profiles of the drugs, and if we don't have a clear winner in terms of efficacy, like a drug here that's going to set the bar significantly higher and stand out from all the rest, the safety profiles are really going to become very important as patients and physicians make choices about therapies. I will say though that for the JAK inhibitors I think they'll be really interesting, especially for patients who are very steroid responsive, corticosteroid responsive because in my personal practice, I've found that some of these patients don't do well on a single targeted biologic, and they may actually need a more broad immunosuppressive therapy like a JAK inhibitor.

Dr. Chovatiya:
Very good point just thinking about the role that JAK and particularly, JAK1 might play across a variety of cytokine families, so this has been the promise with a heterogeneous disease like atopic dermatitis, so I could only hope that maybe we see some similar victories when it comes to HS.

Have there been any particular challenges that have come up when testing a lot of these new HS therapies? I know that you're constantly on the forefront, but anything of note that you feel like has come to your mind about unexpected issues related to the many new potential options?

Dr. Porter:
Yeah. I think one of the things that doesn't get enough attention is that we've actually had a few setbacks in the world of HS therapeutics. One of the things to note is that for psoriasis we're now used to thinking of IL-23 inhibitors as highly efficacious, but we actually had two phase 2 trials for both guselkumab and risankizumab in HS, and both of them either failed to meet their endpoints or were terminated early for failing to meet the endpoints, and so we have a gap now between IL-17 inhibitors being improved and starting these phase 3 trials for JAK inhibitors where the IL-23 inhibitor should have been. And it's a little disappointing because now we'll see risankizumab, for example, got approved for inflammatory bowel disease with an IV loading dose, but I think these drugs didn't work fast enough in HS to really decrease the inflammation or the inflammatory burden that the patients had. And we've had a few other drugs that have gone through some clinical trials that have also been terminated for lack of efficacy.

Dr. Chovatiya:

Before we close, Dr. Porter, are there any final thoughts that you want to share with our audience today when it comes to some of the emerging therapies for HS?

Dr. Porter:
My final thoughts are, number one, I really hope that dermatologists across the country and the world become interested in treating HS, especially with these new therapies. I think in five years we'll be in a much better place, and it will be much easier to just prescribe a medication for HS patients and find that the patients have improved, but until then it's a little difficult sometimes to have to go through trial and error trying to find a medication that will help these patients who really are truly suffering.

Dr. Chovatiya:
And it's really just an exciting time for the treatment landscape of HS in terms of everything we're learning. So with that I just want to thank, Dr. Martina Porter, again for sharing her insights.

Dr. Porter, thanks so much for joining us today.

Dr. Porter:
Yeah, thank you again.

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