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

A Clear Horizon in Plaque Psoriasis: An Update on Investigational Oral Therapies

Announcer:
Welcome to CE on ReachMD. This activity, titled “A Clear Horizon in Plaque Psoriasis: An Update on Investigational Oral Therapies” is provided by Prova Education.

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Dr. Armstrong:
Emerging oral therapies may reshape the current treatment landscape for moderate to severe plaque psoriasis. Today, we'll review recent data in novel oral systemic therapies and their relevance to clinical practice.

This is continuing education on ReachMD, and I am Dr. April Armstrong, professor and chief of dermatology at UCLA. And I'm going to turn to my wonderful colleague to introduce herself.

Dr. Stein Gold:
Well, thrilled to be here. My name is Linda Stein Gold, and I'm the director of dermatology clinical research at Henry Ford Health System in Detroit.

Dr. Armstrong:
Well, Linda, we've seen a lot of developments in the space of oral therapies for plaque psoriasis, and I think we always like to say that the next few years are going to really be the decade of oral therapy development and even a greater development than what we already have. And we've also seen, for example, there are a number of specific oral therapies that are currently in late-phase development. And I want to ask, what are some of the challenges that may still remain in the treatment of psoriasis? And can you briefly review what some of those challenges might be, despite what seems like a lot of different treatment options now available for patients with plaque psoriasis?

Dr. Stein Gold:
So as you mentioned, April, we have this tremendous wealth of options for our psoriasis patients. We're doing great in the biologic arena. We can get the majority of our patients, actually, to clear or almost clear. And in the topical therapy, we have these wonderful new nonsteroidal topicals. And when we look at the oral therapy landscape, right now, we're not quite where we need to be. We still have an unmet need. We have some wonderful new therapies, but we still are not getting the majority of our patients to clear or almost clear.

And some of our challenges are finding these drugs that have that balance of efficacy, safety, and tolerability. We need to give patients medications that they can use and make sure that they have good adherence and making sure that they and the prescribers are

comfortable with these medications.

Dr. Armstrong:
So let's talk specifically about several of these systemic oral therapies under investigation for psoriasis. And, Linda, can you tell us about these?

Dr. Stein Gold:
Absolutely. And as you mentioned, we had a breakthrough apremilast and deucravacitinib being new options that provided potentially safer options in the oral arena. Deucravacitinib is probably the most efficacious of the oral therapies, oral new therapies. We know this is a TYK2 inhibitor that's been shown to be statistically superior to apremilast when studied head-to-head. And I think it's exciting that we have some new TYK2 inhibitors that are also on the horizon

Right now, one of them doesn't necessarily have a name. It's ESK-001. And then there's another one, zasocitinib. I know we've both been involved in clinical trials. I think that these are quite exciting in that they might even provide even higher efficacy than we've seen with deucravacitinib. What do you think?

Dr. Armstrong:
Yes, I think they are really exciting. I was involved, as you were, Linda, in terms of the deucravacitinib trials, and I think that field is going towards can we create an inhibitor that's even more specific to the allosteric domain of TYK2? And this is shown, I think, by the latest development. And can we get even greater consistent coverage in terms of inhibition of TYK2, which is a critical intracellular molecule for mediating the IL-23 pathway.

And so one of the things, I think, that we will be looking at, hopefully, will be unveiled very soon in the next year, is hopefully this phase 3 data for ESK-001 and zasocitinib. I think we're both involved with the clinical trials in terms of these agents, and I think their unveiling will be quite monumental to the field and really help us understand the potential for TYK2 for our oral therapies.

I think when we're looking at ESK-001, for example, in their phase 2 STRIDE study, at week 12, PASI 75 was achieved by 64% of the patients on the highest dose arm, the 40 mg BID, versus 0% in the placebo group. And for zasocitinib, we saw in the phase 2 study that it's PASI 100, about a third of the patients achieving PASI100, which is very encouraging.

Now, let's switch maybe gear a little bit and let's talk about another oral therapy, not a TYK2 inhibitor, but an oral peptide. Linda, can you tell our audience a little bit more about this particular therapy?

Dr. Stein Gold:
Sure. This is an oral IL-23 icotrokinra, or ICO for short. And as you mentioned, this is an oral peptide. This is the first time we're hearing about a peptide for the treatment of psoriasis. This is in between a small molecule and a biologic drug. And the problem with oral peptides is generally they are not absorbed very well. And what's interesting about the structure of ICO is it's a circular structure that actually allows it not to be broken down so much in the GI tract and to have better absorption. And this is highly selective for the IL-23 receptor. And by blocking that receptor, it blocks the downstream signaling of IL-23.

And, April, as you mentioned, this is a key cytokine in the pathogenesis of psoriasis. And there have been a number of preliminary studies looking at this drug versus placebo. I know you've been involved in some of these, and what we're seeing here is a drug that's highly effective as compared with placebo in terms of studying this, actually, in patients age 12 and up. And it was studied versus placebo. It was also studied in areas of high impact like the scalp and genital psoriasis.

Were you impressed, April?

Dr. Armstrong:
Yes. Yes, absolutely. I think when we're looking at the icotrokinra's pivotal studies, the ICONIC-LEAD trial, for example, what we saw was that at week 16, about 65% of patients receiving icotrokinra had achieved clear or almost clear skin versus about 8% in the placebo arm. And then when they looked at PASI 90, which we know is a pretty high bar, what they noticed is that 50% of patients achieved PASI 90 versus 4% with a placebo.

But the key thing that we also noticed with regards to this is that the efficacy continued to go up after week 16. So when we are looking at week 24 data, we have even higher efficacy later on in the clinical trials.

For those just tuning in, you're listening to continuing education on ReachMD. I'm Dr. April Armstrong, and here with me today is Dr. Linda Stein Gold. We're discussing emerging oral systemic therapies for moderate to severe plaque psoriasis.

Now, we know, Linda, this has also been compared with deucravacitinib in the ICONIC-ADVANCE 1 and 2 trial, which was unveiled recently by you at the AAD meeting. So would you like to talk a little bit about some of the findings from that particular study?

Dr. Stein Gold:
I would, actually. And I think whenever we have a new drug, it's really nice to have a head-to-head trial that looks at a drug that we already understand. And as you mentioned in the ICONIC-ADVANCED 1 and 2 studies, we actually have a 3-arm study here. So we have ICO at 200 mg once a day versus placebo, but now we also have an active arm, and this active arm is deucravacitinib at standard dosing, 6 mg once a day.

Unlike the other 2 studies that enrolled adolescents, this was just an adult study. The primary endpoint was at week 16, but we have continued information at this point all the way out to week 24. And what we found was in this head-to-head study, when we look at those patients who got to clear or almost clear, at week 16, about 70% of people on ICO got to clear or almost clear versus up to 54% on deucravacitinib. And as we continue to treat, we see in some cases even better efficacy, up to 74% on ICO versus up to 55% on deucravacitinib.

And what I really find really interesting is when we push harder and we ask for even better depth of response, in fact, complete clearing of the skin, that's where we see even more separation of ICO from deucravacitinib. And we see pretty much a 2-fold grade of response for ICO versus deucravacitinib at both week 16 and week 24

So I think this is really, really impressive. One of the questions you'd have to ask is, what about safety? Whenever we have a new drug, we have to worry about is this safe? And what we found was the overall adverse events through week 24 were lower, actually, in ICO versus deucravacitinib. And when we look at the infection rates, they were comparable to placebo and actually lower than deucravacitinib through week 24.

So I think this is something that kind of fills some of those gaps that we've been missing. We're looking for something that has high efficacy. We're looking for something that has good tolerability. We're looking at something that has predictable safety. And I think in ICO as well as, hopefully, some of these other new molecules, we'll be able to fill that void.

Dr. Armstrong:
That's a great discussion, Linda. And I really like head-to-head studies because they really help to answer specific questions that's done in a very rigorous fashion in terms of the trial design. And I thought this trial was quite informative. As we know, deucravacitinib has served many of our patients extremely well. In this particular study, where we have a newer medication, icotrokinra, and that's been compared in a head-to-head fashion with pretty rigorous endpoints, seeing its superiority in terms of efficacy was quite notable. And this also reminded me of when deucravacitinib was approved, we had the study comparing deucravacitinib versus apremilast in the POETIC studies with deucravacitinib, where we had apremilast was the active control arm and in showing the superiority.

So I think it really shows a bit of evolution in terms of our field in the oral therapy realm, where we are continually advancing and really looking at therapies and how their promise and the potential of really giving that an additional advancement and an additional efficacy for our patients in the future. So this is all very, very exciting.

Now, let's continue on and really think about some of the clinical impact for some of these data that we just talked about, not only deucravacitinib, but also zasocitinib, ESK-001, and also with regards to icotrokinra that we just talked about. Can you tell us about your thoughts about impact of this clinical data and how they may shape our practice in the future?

Dr. Stein Gold:
Yes. I think these are really very, very important additions. Hopefully they will get FDA-approved because when we ask patients what they want, and we've done a number of studies looking at this, it turns out for patients who have moderate or severe disease, when you

ask them what form of administration would you prefer, most patients actually prefer an oral option. And I know, as you mentioned in the past, that we've had oral options, but they weren't necessarily the safest options. Now we have options that provide us with much better efficacy, much better safety, much better tolerability. So I think that these are going to be an important option that we will ask our patients about. And for those patients who prefer an oral agent, I think these are going to be really, really great options for them to get their plaque psoriasis under control.

Dr. Armstrong:
Absolutely. I think that when we're thinking about moderate to severe plaque psoriasis, especially I would say for our younger patients—as we know, some of these trials are down to age 12—for example, in the icotrokinra studies that we mentioned where the data had been revealed, it's oftentimes very helpful to be able to offer that oral option to our younger patients.

Well, this has certainly been fascinating, and it's always great to talk with you, Linda, about these newer therapies. And before we wrap up, can you share with our audience your one take-home message?

Dr. Stein Gold:
I think my one take-home message would be to make sure that you stay up to date with the new science and the new treatment options that come available. We have some wonderful options that are on the horizon, and we really owe it to ourselves and our patients to make sure we understand the benefits that these medications can provide for our patients and make sure that we consider them when discussing therapeutic options with our patients.

Dr. Armstrong:
That's a great message. And if I may add one message from this particular recording is that we are having newer TYK2 inhibitors that will hopefully be available to us very soon, and hopefully their phase 3 trial results will be unveiled. And we have an IL-23 receptor oral agent where we've already seen phase 3 results, and hopefully we'll be seeing that being available soon for our clinicians as well.

Well, and that's all the time we have today. So I want to thank our audience for listening and thank you, Linda, for joining me and sharing your valuable insights.

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