



What's coming down the psoriasis pipeline?

Experts break down emerging treatment options
and what they can offer patients and physicians.



BY EMILY MARGOSIAN, ASSISTANT EDITOR

While a permanent, perfect solution for psoriasis remains elusive, treatment advances over the past decade have helped dermatologists and their patients get one step closer to clear skin. Currently, the FDA has approved 11 biologics and 12 biosimilars for the treatment of psoriasis (two for etanercept, six for adalimumab, four for infliximab), as well as a PDE-4 inhibitor (apremilast).

These existing treatments work well and are considered safe. However, new drugs in the pipeline may offer greater efficacy, and add to the expanding arsenal of biologic, oral, and topical options that patients may choose from. >>



What's coming down the psoriasis pipeline?

Biologics

Currently, there is one new biologic in late-stage development for the treatment of psoriasis. Bimekizumab, manufactured by UCB, is presently in phase 3 clinical trials, and is anticipated to be available by October 2021.

Mechanism of action

“Bimekizumab is a monoclonal antibody biologic that targets IL-17A and IL-17F. We don't currently have any other type of drug that blocks those two cytokines,” explained Andrew Blauvelt, MD, MBA, FAAD, president of Oregon Medical Research Center. Dr. Blauvelt has served as a clinical study investigator and scientific advisor for UCB Pharma. “Although it will be placed in the IL-17 blocker class, in which we have three drugs already, it's unique in that it blocks IL-17A and IL-17F.”

Bimekizumab's unique mechanism of action is likely linked to its positive performance in clinical trials, suggested Paul Yamauchi, MD, PhD, FAAD, clinical assistant professor of dermatology at the University of California, Los Angeles, and a consultant and investigator for UCB. “The current IL-17 inhibitors, like ixekizumab and secukinumab, just target IL-17A, but bimekizumab targets both A and F, and it's been shown that both IL-17A and IL-17F are implicated in the pathogenesis of psoriasis. Also targeting IL-17F could explain the higher efficacy of bimekizumab to treat psoriasis,” he explained.

Dosing

Frequency of administration could be as little as once every eight weeks, said Jerry Bagel, MD, MS, FAAD, director of the Psoriasis Treatment Center of New Jersey, clinical professor of dermatology at Mount Sinai School of Medicine, and consultant for UCB. “Either once every four, or once every eight weeks,” he said. “The data showed that once every eight weeks — I believe it was 320 milligrams — worked comparable to every four weeks after the initial loading dose.”

Efficacy

So far, clinical studies of bimekizumab have shown greater efficacy in head-to-head trials with other IL-17 blockers. “Bimekizumab seems to have at the very least, a slightly higher efficacy than the other two — definitely higher than secukinumab, and I believe slightly higher than ixekizumab,” said Dr. Bagel, who has served as a consultant for Novartis and Eli Lilly. “With bimekizumab, your PASI 100 gets as high as 67%; that's two out of three people on bimekizumab who are going to be clear. That's higher than I've ever seen data before for any drug.”

Bimekizumab has also shown exciting potential for the treatment of psoriatic arthritis, according to Dr. Blauvelt. “That's the exciting part about it. With psoriatic arthritis, we've been stuck for a while at making advances, and this drug appears to move the needle to a much higher bar of efficacy. So, it's a slight increase compared to other biologics for skin efficacy, but it's a significant increase for efficacy on joint disease.”

Safety considerations and adverse events

While the additional blockade of IL-17F has yielded greater efficacy in clinical trials, it has also produced a greater occurrence of oral thrush. “Candidiasis is a class effect among the IL-17 inhibitors, but it's seen at a lower rate with secukinumab and ixekizumab — single-digit incidence compared to 15% on the average with bimekizumab,” explained Dr. Yamauchi. “The feeling is that maybe because it also targets IL-17F, there's a higher signal for oral candidiasis.”

However, most cases are mild to moderate and do not interfere with continuation of the drug, according to Dr. Blauvelt. “I believe that particular side effect will be manageable in most patients,” he noted.

From a positive safety standpoint, although other IL-17 blockers have been linked to a slight increase in exacerbation of inflammatory bowel disease such as ulcerative colitis and Crohn's, those side effects have



What's happening with biosimilars?

Currently, there are several FDA-approved biosimilars for the treatment of psoriasis and psoriatic arthritis:

Adalimumab biosimilars:

1. adalimumab-atto (Amjevita)
2. adalimumab-afzb (Abrilada)
3. adalimumab-adbm (Cyltezo)
4. adalimumab-bwwd (Hadlima)
5. adalimumab-fkjp (Hulio)
6. adalimumab-adaz (Hyrimoz)

Etanercept biosimilars:

1. etanercept-szsz (Erelzi)
2. etanercept-ykro (Eticovo)

Infliximab biosimilars:

1. infliximab-axxq (Axsola)
2. infliximab-dyyb (Inflectra)
3. infliximab-qbtx (Ixifi)
4. infliximab-abda (Renflexis)

While the rollout of biosimilars has been a slow process, Dr. Bagel anticipates that they will become a bigger part of the psoriasis treatment landscape soon. "I mean, adalimumab biosimilars are here. There are biosimilars of ustekinumab that are in development, and IL-17 biosimilars are in development as well. So that's something to keep in mind also, even though it's not as sexy as some of the newer products," he said. "In my opinion, biosimilars for the most part, seem to be pretty close to as efficacious as the originators. Eventually, I'm sure the insurance companies are going to clamp down on us to start using them. I think people at least need to know that they're in development, and they're in the pipeline."

Potential concerns about interchangeability between a biologic and a biosimilar have been assuaged in recent studies, so long as the biosimilar has been designated by the FDA as interchangeable with the prescribed biologic for the specified indicated use. "It's very safe and effective, is the bottom line," said Dr. Blauvelt. "The testing of biosimilars has shown that they are as safe and as effective as the original biologics. Many of the trials have also shown that you can switch easily and safely between biosimilars and originator biologics. In fact, that's the requirement of a biosimilar to be on the market — it has to show similar safety and efficacy as the originator. Otherwise, it would not be approved by the FDA. If it makes it through the regulatory process, physicians should be comfortable with the efficacy and safety of biosimilars."

Whether or not the promise of cost savings with biosimilars will pan out is less certain, however. "The promise of biosimilars is very attractive, in that everyone wants to have a lower-priced biologic to increase access. What we're seeing, however, in the United States is that the cost reductions are only in the 10-20% range compared to the originator," explained Dr. Blauvelt. "We're not seeing an increase in access due to that minor cost decrease, which undermines the promise of biosimilars. On the other hand, in European countries, we've seen 50-70% reductions in the cost of biosimilars, which has led to more widespread use of biosimilars in patients, and more widespread use of biologics in patients in general. If it translates to more people getting them because they're cheaper, awesome. Unfortunately, that has not yet been realized in the United States."



What's coming down the psoriasis pipeline?

not been observed in clinical trials of bimekizumab. “The good news is it really didn’t show up with bimekizumab. I don’t know if it’s going to be included as a class effect by the FDA or not, but the data did not reflect an increase as it may have showed in the other three IL-17 blockers,” said Dr. Bagel.

Oral drugs

There is currently one new oral drug for psoriasis in the pipeline. Deucravacitinib, manufactured by Bristol-Myers Squibb, is currently in phase 3 clinical trials and is estimated to come to market sometime in 2022.

Mechanism of action

“Deucravacitinib is an oral small molecule inhibitor of TYK2. TYK2 is a member of the JAK family of signal transduction tyrosine kinases. The reason why TYK2 is an attractive target for psoriasis is because TYK2 is involved in the signaling of IL-23,” explained Dr. Blauvelt, who has served as a clinical study investigator and scientific advisor for Bristol-Myers Squibb. “There are other cytokines that utilize TYK2 signaling, and those include interleukin 12 and type 1 interferons, but most people believe that the main anti-psoriatic activity of this drug comes from blocking the signaling of IL-23, which we know is an important target in psoriasis. We currently have three IL-23 blocker biologics on the market — risankizumab-rzaa, guselkumab, and tildrakizumab-asmn — so this is, if you will, kind of an oral version.” Dr. Blauvelt has also served as a clinical study investigator and scientific advisor for AbbVie, Janssen, and Sun Pharma.

Dosing

In phase 3 trials, deucravacitinib was administered at a dosing of 6 mg once daily.

Efficacy

In phase 3 trials, approximately 55% of patients achieved PASI 75 at week 16 with deucravacitinib. “Those studies were head-

to-head with apremilast, which showed efficacy in the same study of 35-40% PASI 75 at week 16. So, the drug was clearly shown to be superior to apremilast in the two recently reported phase 3 studies,” said Dr. Blauvelt. “The value of deucravacitinib is that we will have a new oral drug option with better efficacy than apremilast, which is a common oral treatment used for psoriasis. On the other hand, even though it’s an exciting advance in terms of oral therapy for psoriasis patients, the efficacy still does not compare with the best biologics we have on the market.” Dr. Blauvelt has served as a clinical trial investigator and scientific advisor for Amgen.

Dr. Bagel looks forward to improved oral treatment options for psoriasis patients who may not want to pursue a biologic. “I think the real question when you’re in the trenches with your patients will be, ‘do you want to take a pill once a day that works, let’s say, 60% of the time, or do you want to take a shot that works 90% of the time?’ That’s going to be an interesting discussion once we have that available, because we’ve never had an oral medication that works as well as a biologic,” he said. “However, something like deucravacitinib that works as well as ustekinumab or adalimumab, at least gives a fighting chance if somebody just wants to take a pill instead of a shot. The efficacy is not going to be as high as some of the high-flying biologic agents, but many people may think that an oral medication is safer and be more willing to take it. This one is good enough to at least compete.” Dr. Bagel has served as a scientific advisor for AbbVie, Amgen, and Janssen.

Safety considerations and adverse events

Compared to other JAK inhibitors, deucravacitinib has a good safety profile, according to Dr. Yamauchi, who has served as a consultant and investigator for Bristol-Myers Squibb. “The only side effects have been acne and folliculitis, in about 2% of subjects, which is pretty low impact for

me,” he said. “The good thing about deucravacitinib is that there were no laboratory abnormalities seen in clinical trials, and no serious infections. In other words, deucravacitinib did not display the black box warning events that the JAK inhibitors are associated with,” he said.

Dr. Bagel agrees that, thus far in clinical trials, deucravacitinib appears to have limited side effects. “There’s no increase in malignancies, serious infections, yeast infections, ulcerative colitis, or Crohn’s disease. You’re looking at a safety profile that, in my opinion, so far looks pretty good.”



Another door opens?

Read more about what the FDA approval of multiple JAK inhibitors could offer dermatology patients at www.aad.org/dw/monthly/2021/may/feature-another-door-opens.

Topicals

There are two new topicals for psoriasis currently in the late-stage pipeline, tapinarof and roflumilast. Tapinarof is manufactured by Dermavant, and in May 2021, the company submitted a new drug application (NDA) to the FDA. Roflumilast is manufactured by Arcutis and is currently in phase 3 studies.

“Both are non-steroidal, topical applications for psoriasis, which means they can be used anywhere on the body,” explained Dr. Bagel. “With topical steroids, you have to worry about thinning of the skin and atrophy, which could occur more frequently on the face, under the arms, under the breasts, or in the groin. There are certain times when you’re going to have to write two or three different prescriptions for somebody. In a nonsteroidal application, if it’s efficacious, you only have to use one.”

Navigating access issues

While new drugs offer the promise of greater treatment potential, they may very likely be out of reach for the patients who need them most. “Access is a very important topic. For all these new psoriasis drugs entering the market, access is going to be restricted. This has been our experience with all new drugs that come to market for skin diseases,” explained Dr. Blauvelt. “Due to the high cost, they’re often tiered behind cheaper alternatives. Dermatologists often must work harder in terms of paperwork and telephone calls to get access to some of the newer medicines that their patients need. There are currently many states that have either passed or will pass legislation placing restrictions on step-therapy protocols that are put into place by payers. I hope that these legislative efforts are successful, so that it will be easier to treat our patients with the drugs that we want to use to treat them.”

Access Academy resources on navigating issues with private payers, including:

- A private payer appeal letter generator: www.aad.org/member/practice/drugs/private-payer/payer-tool
- A prior authorization letter generator: www.aad.org/member/practice/drugs/pa-tool
- The AADA Prior Authorization Resource Center: www.aad.org/member/practice/drugs/pa-resources
- Step therapy guidance: www.aad.org/member/advocacy/state/step



What's coming down the psoriasis pipeline?

Tapinarof

Mechanism of action

“Tapinarof is an aryl hydrocarbon receptor agonist (AHR). AHR induces broad anti-inflammatory activities within the skin. The interesting thing about this drug is that it is a non-steroidal, new topical option for patients with more limited skin disease,” said Dr. Blauvelt, who has served as a clinical study investigator and scientific advisor for Dermavant.

Dosing

Tapinarof is a topical cream applied once daily.

Efficacy

In preliminary studies, efficacy was equivalent to that of topical steroids according to Dr. Blauvelt. “This drug has the potential to induce long-lasting clearance of skin lesions based upon initial data that has been reported.”

Dr. Bagel agreed that tapinarof is a good candidate as a comparable alternative to topical steroids. “It works well. It gives you a PGA clearance of 0 or 1 at 65%, in about 12 weeks. It may work a little slower than some of the steroidal class 1 super potent steroids for sure, but 65% PGA is really good. From what I've seen, it's one of the higher efficacious molecules around.”

Safety considerations and adverse events

The primary side effect associated with use of tapinarof is folliculitis, particularly in the areas surrounding the treated plaques. “There wasn't much burning, stinging, or irritation, but folliculitis for some reason did appear,” said Dr. Bagel.

Roflumilast

Mechanism of action

“Roflumilast is a PDE-4 inhibitor, similar to crisaborole which is approved for atopic dermatitis, and apremilast which is approved for psoriasis,” explained Dr. Blauvelt, who

has served as a clinical study investigator and scientific advisor for Arcutis and Pfizer. “The advantage of this drug is that it appears to be a much more potent blocker of PDE-4, compared to both of those drugs when tested in the laboratory.”

Dosing

Like tapinarof, roflumilast is a once-daily topical cream. “In trials, it was applied up to eight weeks, but I think that with this product, patients can apply indefinitely, and also it can be applied safely on the sensitive areas of the body.” said Dr. Yamauchi, who has served as a consultant and investigator for Arcutis.

Efficacy

“The efficacy of this product is comparable to a mid-potency steroid. By week eight, over half the patients met the primary endpoint of being almost clear. The placebo rate was also pretty low, so this product will likely show benefit as a non-steroidal agent to treat psoriasis,” said Dr. Yamauchi.

Dr. Bagel is curious to see how the efficacy of roflumilast bears out as it continues to be evaluated in clinical trials. “It's almost a little like crisaborole; PGA of 0 or 1 is about 40%. It still has efficacy and there's potential there, so it's something to keep in mind as it gets developed,” he said.

Safety considerations and adverse events

According to Dr. Yamauchi, thus far, roflumilast has little to no side effects. “Really nothing,” he said. “No tolerability issues, no stinging or burning. It's a pretty tolerable drug without any significant adverse events.” **DW**