Transcript Details
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Mental Health Implications in Psoriasis

Neil Bhatia, MD:
Hi, I'm Dr. Neil Bhatia. I'm Chief Medical Editor of *Practical Dermatology*, and welcome to another installment of the IL-17 Journal Club. I'm here with my friend Andy Blauvelt, who needs no introduction. But Andy, give us an update on where you are and what you're doing these days.

Andy Blauvelt, MD:
Hi, everybody. My name's Andy Blauvelt. I'm a dermatologist and a consultant for Blauvelt Consulting, LLC—my single-member consulting firm. I spent 19 years in academics and then 13 years conducting clinical trials at Oregon Medical Research Center in Portland. Today, we're going to be talking about bimekizumab. I was an investigator for all the bimekizumab trials and an author on many of the publications.

Neil Bhatia, MD:
Absolutely—that's great work, and we appreciate it. But more importantly, can you talk a little bit about IL-17? We're hearing so much about where IL-17 is fitting in now across multiple disease states outside of psoriasis. Give us an overview of your understanding of its impact on neurogenic and psychogenic pathways, specifically what we're seeing with depression and suicide.

Andy Blauvelt, MD:
Yeah, this goes back to the brodalumab trials, Neil. As you know, we were in the middle of phase III with brodalumab—everything was going swimmingly—and then all of a sudden the whole program was stopped midstream. It was stopped because there were four suicides that occurred during the phase III program, and the company felt it was too risky to continue. Eventually, brodalumab did make it to market through another company, but that really stirred things up.

What's interesting is that prior to that, we already had two IL-17A blockers—secukinumab and ixekizumab—and we really didn't see much in terms of suicide or mental health issues. So the brodalumab result was pretty shocking, and it made people wonder whether there was something different about targeting the cytokine itself, as with secukinumab and ixekizumab, versus targeting the receptor, as with brodalumab. There are theories out there, but I don't think anyone really knows for sure.

Neil Bhatia, MD:
I've always been puzzled by that as well. Why would receptor blockade—when you're not depleting the cytokine itself—create such a difference compared to directly targeting IL-17? And as you said, there were only four cases, many of which occurred several hundred days off drug. A couple happened shortly after leaving the trial, and unfortunately, they were all at one site. It also brings up our current trial paradigm with the Columbia Scale and other assessments. Have you seen any updates on broader mental-health impacts, even beyond suicidality?

Andy Blauvelt, MD:
Yes. What the brodalumab experience did was heighten FDA concern when bimekizumab came along. The FDA required UCB to conduct much more intensive suicide monitoring than in prior IL-17 studies. In the bimekizumab trials, there were the ECSSR and PHQ questionnaires, both asking very similar questions—"Are you suicidal?" "Have you had suicidal thoughts?"

Patients were questioned frequently, sometimes monthly. In fact, some of my patients complained about being asked these questions every month—"What's the deal here?" It actually became a negative aspect of the trial for them. As a result, there were some positive responses to these questions. The FDA interpreted the data cautiously and included warning language in the bimekizumab label, although it did not include a boxed warning.

Neil Bhatia, MD:
Which is important, because that boxed warning has unfortunately labeled brodalumab as "the suicide drug," which I think is unfair. Another issue is that, occasionally, these screenings uncover patients with depression or suicidal ideation, and then those patients are disqualified from trials—which is an unfortunate outcome.

Andy Blauvelt, MD:
Exactly. As many people know, psoriasis itself is associated with an increased risk of mental-health issues, including suicide. Patients with psoriasis have higher rates of depression, anxiety, sexual dysfunction, relationship problems, and work impairment. I always say psoriasis really has a huge impact on mental health.

So you start with that baseline risk, then add intensive monitoring in trials. Over the years, we've occasionally seen suicides in these programs. One key point I want listeners to understand is that last year we published a paper in the *Blue Journal* examining mental-health outcomes with bimekizumab. For me, the most important part of that paper is Supplemental Figure 1.

In that figure, we show rates of suicidal ideation, suicide attempts, and completed suicides with bimekizumab and compare them with ixekizumab and secukinumab (grouped as IL-17A blockers), brodalumab separately, and then all IL-23 blockers grouped together. The only signal that clearly stands out is brodalumab, with the four completed suicides.

The bottom line is that bimekizumab's data fall right in line with ixekizumab, secukinumab, and the IL-23 blockers. It doesn't stand out. Unfortunately, the FDA still chose to include warning language in the label. It's not a boxed warning, but I disagree with it based on the data.

Neil Bhatia, MD:
I completely agree. It's no different from what we see with JAK inhibitors—patients Google things and we're constantly playing defense. These warnings are guidance, not prohibitions. They don't mean "never prescribe these drugs"; they mean we should pay attention.

At the same time, we see how efficacious these therapies are and how dramatically they change lives. I always say the cost of *not* treating patients is far worse than the cost of treating them. And I'm sure you've—

Andy Blauvelt, MD:
Absolutely. And that point is way under-emphasized. All the mental-health measures we track actually improve with these drugs—including brodalumab. Quality of life improves significantly, anxiety decreases, depression decreases, work performance improves. Instead, we focus on a few isolated suicide cases and analyze them endlessly. The reality is that we're helping far more people than we're harming.

Neil Bhatia, MD:
You've been one of the pioneers in medical dermatology—your name is on countless papers, and your NIH work and time in Oregon were remarkable. If you had to give colleagues one take-home message about not losing medical dermatology and being appropriately aggressive, what would you say?

Andy Blauvelt, MD:
Unfortunately, we still see a lot of undertreatment of psoriasis, and it really breaks my heart, because we have such great therapies now. I believe IL-23 and IL-17 blockers should be our mainstay. I no longer recommend TNF blockers. IL-23 blockers work extremely well for skin-only disease, and IL-17 blockers are excellent for psoriatic arthritis.

These drugs are highly efficacious, safe, and convenient. Number one: use them. Number two: don't wait too long. There's increasing evidence that earlier treatment leads to higher PASI 100 rates, greater clearance, and longer remissions. Cycling through A, B, and C before getting to the best drugs only delays optimal care. Use these therapies earlier—that's how you give patients the best life possible.

Neil Bhatia, MD:
Well said. We're seeing similar trends in hidradenitis and soon in urticaria as well. Psoriasis has truly led the way. Thank you, Andy, for everything you've done, and thanks for spending time with me today.

Andy Blauvelt, MD:
You're welcome, Neil. Thanks for having me.

Neil Bhatia, MD:
All right.