Transcript Details

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IL-17A Inhibition and the Stress Response in Psoriasis

Ryan Quigley:
When we prescribe secukinumab for moderate-to-severe psoriasis, we're usually focused on one thing: neutralizing IL-17A to shut down the inflammatory cascade driving plaques. But what if blocking IL-17A also sends signals beyond the skin?

You're listening to *AudioAbstracts* on ReachMD. I'm Ryan Quigley, and today, I'll be talking about a study that investigated how the IL-17A inhibitor secukinumab impacts the body's stress response—also known as the hypothalamic pituitary adrenal, or HPA, axis.

The study was conducted over 16 weeks, and 105 patients with psoriasis received either standard 300 milligram dose of secukinumab or a reduced dose at 75 milligram. In addition to tracking clinical outcomes, investigators measured plasma levels of IL-17A, cortisol, adrenocorticotropic hormone also called ACTH, prolactin, dehydroepiandrosterone or DHEA, and perceived stress scores with the primary goal being to see whether IL-17A inhibition influences the HPA axis.

Pharmacologic studies showed that circulating IL-17A levels increased significantly after starting secukinumab in both dosage groups. And this is in line with what previous studies saw as well, even though it might sound paradoxical. When IL-17A binds to secukinumab, its clearance is reduced, leading to higher measurable total IL-17A levels in plasma. For both doses, circulating IL-17A increased from roughly 6 picograms per milliliter at baseline to around 40 to 50 picograms per milliliter by week 16. And importantly, this increase was dose-*independent,* which is consistent with prior data.

But here's where things get interesting.

Cortisol levels also rose significantly in both groups—by approximately 33 percent over 16 weeks for both doses. This suggests measurable activation of the HPA axis during IL-17A inhibition. Baseline cortisol levels averaged around 170 nanomoles per liter, increasing to roughly 222 to 234 nanomoles per liter at follow-up.

ACTH also increased significantly in the 75 milligram group, but not the 300 milligram group, and DHEA levels showed a small overall increase across the cohort, reaching statistical significance in pooled analyses, although subgroup effects were inconsistent and modest. Prolactin, however, remained stable.

So what does this mean?

Psoriasis has long been associated with stress-system dysregulation. Prior studies have shown that patients—especially those reporting high stress—can exhibit relatively blunted cortisol responses, possibly reflecting chronic HPA activation and functional exhaustion. In this study, baseline data supported that concept: perceived stress inversely correlated with cortisol levels.

During treatment, that relationship shifted. The negative correlation weakened and, in some analyses, even became positive. While not uniformly significant across groups, the pattern raises the possibility that secukinumab may be normalizing—or at least modulating—HPA axis responsiveness.

However, the rise in cortisol did *not* correlate with improvements in PASI or DLQI scores. Clinical response, particularly at 300 milligrams, where almost 86 percent achieved a PASI score of less than three by week 16, appears to be driven primarily by IL-17A blockade itself—not by endocrine changes. That suggests HPA activation is more likely a secondary or supportive phenomenon rather than a primary therapeutic driver.

But before we dismiss it, let's consider the systemic implications.

Sustained cortisol elevation—even at moderate levels—can influence glucose metabolism, bone density, adiposity, and cardiometabolic

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risk. This matters in psoriasis, where baseline cardiovascular risk is already elevated. A 16-week study can't determine long-term consequences, but it raises important questions about chronic immune–endocrine cross-talk during biologic therapy.

Mechanistically, we don't yet know whether IL-17A inhibition directly influences the HPA axis, or whether reduced systemic inflammation decreases stress burden and resets feedback loops. Both pathways are biologically plausible.

As we increasingly treat inflammatory disease with targeted biologics, understanding these systemic ripple effects may become just as important as clearing the skin.

This has been an *AudioAbstract*, and I'm Ryan Quigley. To access this and other episodes in our series, visit ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

Reference:

Krefting F, Hölsken S, Sondermann W, Schedlowski M. Hypothalamic pituitary adrenal axis hormone changes during IL-17A inhibition with secukinumab in patients with psoriasis. *Clin Immunol*. 2026;282:110611. doi:10.1016/j.clim.2025.110611

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