Tralokinumab: A New Potential for Atopic Dermatitis

New biologic therapy tralokinumab, a human monoclonal antibody targeting IL-13, is under FDA review for the treatment of atopic dermatitis.

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Jonathan Silverberg, MD, PhD, MPH, associate professor of dermatology at George Washington Medical School in Washington, DC.

A new biologic for treating moderate to severe atopic dermatitis (AD) could come to market within the next year. The FDA in July accepted LEO Pharma's Biologics License Application for tralokinumab, an IL-13 inhibitor, starting the clock on a review process that is set to conclude in the second quarter of 2021.[1]

Physicians are eager to have a new weapon in the arsenal to treat this debilitating disease, said one dermatology expert.

"As a clinician, you always want more options," explained Jonathan Silverberg, MD, PhD, MPH, associate professor of dermatology at George Washington University School of Medicine and Health Sciences in Washington, DC. "It's not to say that our current options are not good ones, but we always need more and potentially better options. We're excited to have new therapies."

If approved, tralokinumab, which also is under review in Europe, would become the second biologic to treat AD.

Dr Silverberg believes payers would welcome an additional biologic for this disease. "There's still a lot of unmet need for more therapies. There definitely will be a role for this product in the marketplace."

AD affects an estimated 13% of children and 7.2% of adults in the United States.[2] Symptoms include severe itch, pain, and lesions, and AD is associated with mental health issues.

Traditional treatments for AD include topical corticosteroids to ease inflammation, tar treatments to reduce itching, and phototherapy. In addition, two topical immunomodulators, pimecrolimus and tacrolimus, are available to treat mild to moderate AD.

More Targeted Approach to Treatment

Tralokinumab is the latest to target proteins involved in the disease state. Dupliumab, which blocks the IL-4 receptor alpha subunit, was approved in 2017.[3]

Once it was understood that AD is an immune disease, and patients with moderate to severe disease may need systemic treatments, it paved the way to a different type of approach that is more targeted, explained Emma Guttman-Yassky, MD, PhD, Sol and Clara Kest Professor of Dermatology, director of the Center for Excellence in Eczema and Laboratory of Inflammatory Skin Disease, and the upcoming system chair of the department of dermatology at the Icahn School of Medicine at Mount Sinai Medical Center (New York City, NY). "Until recently with the approval of dupilumab that targets both IL-4 and IL-13, all the systemic treatments we had for AD were nonspecific. It is great to have additional specific drugs for AD," she said.

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> *—Dr Silverberg*

Andrew Blauvelt, MD, MBA, president of Oregon Medical Research Center in Portland, has treated a number of patients with dupilumab. In clinical practice, he said, "patients achieve mean [Eczema Area and Severity Index (EASI)] score reductions of around 80%, while quality of life measures also improve."

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Emma Guttman-Yassky, MD, PhD, Sol and Clara Kest Professor of Dermatology, director of the Center for Excellence in Eczema and Laboratory of Inflammatory Skin Disease, and the upcoming system chair of the department of dermatology at the Icahn School of Medicine at Mount Sinai Medical Center in New York City, NY.

Dr Blauvelt added that "the [Investigator Global Assessment (IGA)] goal of 0 to 1, minimal or no disease, set by the FDA represents a very high bar—in more real-life terms, most investigators estimate that about 90% of their patients are successful and happy with the drug."

Dr Silverberg pointed out that with dupilumab, "we have a targeted option that has a better safety and efficacy profile for long-term management of the disease."

Tralokinumab Targets IL-13

Tralokinumab is a fully human monoclonal antibody that specifically neutralizes the IL-13 cytokine, a key driver of the underlying inflammation in AD.

If approved, it would become the first biologic to specifically neutralize the IL-13 cytokine, said Kim Kjøller, MD, executive vice president of global research and development at LEO Pharma. The therapy offers a "more targeted approach for adults living with this debilitating disease," Dr Kjøller said.

Clinical trial results of tralokinumab were presented at the American Academy of Dermatology Virtual Meeting Experience 2020, held in June.[4,5] This included safety and efficacy data from the pivotal phase 3 trials ECZTRA 1, ECZTRA 2, and ECZTRA 3, which tested tralokinumab monotherapy or tralokinumab with concomitant topical corticosteroid use in adult patients with moderate to severe AD.

Dr Silverberg presented on tralokinumab with concomitant topical corticosteroid, reporting results from the 32-week phase 3 ECZTRA 3 trial.[4] In that trial, roughly 39% of patients achieved IGA 0 mark by week 16. Furthermore, roughly 56% of patients achieved a 75% improvement of the EASI from baseline at week 16, Dr Silverberg noted. Regarding reductions of itch, 45% of patients achieved a four-point response of their worst daily itch, which is considered by the FDA to be clinically meaningful response in itch, he added.

Overall, tralokinumab achieved significantly higher rates of clear skin or almost clear skin, along with significant improvements of other clinician-reported end points, including intensity of itch over time and improvements in quality of life.

"We're seeing across the entire gamut of end points that tralokinumab is effective and is improving the overall disease state for AD patients," Dr Silverberg said, adding that tralokinumab offers a topical "steroid-sparing" effect. Patients in the tralokinumab arm used significantly less topical corticosteroids compared with those in the placebo arm.

Super Responders

Similar to those in clinical trials, some of Dr Silverberg's patients are so-called "super responders," whose AD and itching clear almost immediately. "Others may take weeks or months to reach 50% to 90% improvement," he said. "At this time, it's impossible to predict with accuracy how any particular individual will respond." He added that "some patients do better on weekly dosing than those dosed every other week, although it's challenging to get insurance coverage for weekly dosing."

Clinical trials of tralokinumab examined dosing every other week and either with topical steroids or without topical steroids.

Dr Silverberg conceded it's unknown what would happen if tralokinumab was dosed more frequently or at a higher dose. "In theory, it's possible that more efficacy would be achieved, but that wasn't studied in this study," he said.

It's also not possible to say how tralokinumab compares to dupilumab, Dr Silverberg added, as the studies were not head-to-head trials. "I think at high level what we can say is that tralokinumab looks like it works well, and that it will be an important addition to our therapeutic armamentarium," he said. "I think where it can exactly fit, we're going to have to see over time, and we'll get more real-world data to sort some of that out." ■

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