

# The Atopic Dermatitis Biologic Era Has Begun



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**A**topic dermatitis (AD) is a vexing multisystem disorder characterized by frequently recurrent, intrusive, and sometimes disabling itch and dermatitis. The itch may be present throughout the day but crescendos at bedtime or 1 to 2 hours after sleep initiation, resulting in disrupted sleep cycles, lack of rest, more hours scratching, daytime somnolence, poor work attendance and performance, and poor school attendance and performance.<sup>1</sup>

Atopic dermatitis is a lifelong disease that only remits in approximately half of patients.<sup>2</sup> There is a need for a disease-specific systemic drug in AD. Phototherapy, cyclosporine, methotrexate, and azathioprine are nonspecific immunosuppressive agents that can be used off label for AD but may or may not be effective.<sup>3</sup> Oral or intramuscular corticosteroids are associated with problematic side effects such as weight gain, osteoporosis, fractures, psychological problems, striae, buffalo hump, and steroid withdrawal symptoms and disease aggravation upon withdrawal (ie, flaring to a state worse than prior to steroid initiation).<sup>3,4</sup>

A biologic medication for AD has been long overdue. Psoriatic biologic medications have been tried in AD with occasional benefit in case reports but no major response in larger trials. Belloni et al<sup>5</sup> reviewed early data on off-label usage of biologics approved by the US Food and Drug Administration for psoriasis or other indications applied to AD patients. In their review of cases, they make the point that results are variable and anti-B-cell activity may hold the greatest promise.<sup>5</sup> On the other hand, a recent series of 3 patients showed limited response to rituximab in chronic AD,<sup>6</sup> while a combination of omalizumab, an anti-IgE medication, and rituximab was helpful in some patients.<sup>7</sup> Ultimately, the issue is that

nonspecific biologics may or may not address the underlying disease factors in AD. Therefore, there has been a true need for biologic intervention targeted directly at the pathogenic mechanism of AD. Furthermore, the desire for a biologic targeted at AD is paired with the true need to have a medication so targeted that the drug would have little effect on the rest of the immune system, resulting in targeted immunomodulation without secondary risk of infections.

Wait no longer, that era arrived a few months ago with the rapid US Food and Drug Administration approval of dupilumab, an injectable medication used every 2 weeks for the therapy of moderate to severe AD. This fully human monoclonal antibody against the IL-4R $\alpha$  subunit blocks IL-4 and IL-13, key inflammatory agents in the triggering of production of IgE and eosinophil activation. Even better than the fact that it is targeted are the excellent outcomes in the therapy of moderate to severe AD in adults and the minimal side-effect profile resulting in no requirements for laboratory screening or ongoing monitoring.<sup>8</sup>

Dupilumab seems to perform well, both clinically and in improving the lives of AD patients. Meta-analysis of trials involving dupilumab has shown improved health-related quality of life outcomes.<sup>9,10</sup> Usage of dupilumab alone in clinical trials for 16 weeks (SOLO 1 and SOLO 2) has resulted in stunning reduction in disease severity with a limited side-effect profile, with patients most commonly reporting conjunctivitis.<sup>11</sup> In real-world models where dupilumab is added into a regimen of topical corticosteroid usage (LIBERTY AD CHRONOS trial), patients fared even better with the combination, highlighting that this medication may best be used adjunctively to our skin care guidance as dermatologists.<sup>12</sup>

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A new era for AD patients has arrived and we as practitioners are now fortunate to be able to therapeutically reach the worst cases of AD. The new era has only begun with dozens of new agents addressing a variety of interleukin pathways including IL-17 and IL-22 still under development. Ultimately, we hope that ongoing pediatric trials will allow us to glean the role of early disease intervention at the root cause of AD and address our abilities to prevent comorbidities and disease persistence. Will we be able to avert years of disabling disease? The future holds immense hope.

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