DERMATOLOGY

Openventio PUBLISHERS

ISSN 2473-4799 Open Journal http://dx.doi.org/10.17140/DRMTOJ-2-e003

Editorial

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Volume 2 : Issue 2
Article Ref. #: 1000DRMTOJ2e003

Article History
Received: October 24th, 2017
Accepted: October 25th, 2017
Published: November 20th, 2017

Citation
Howell MD. Emerging age of opportunity for more effective treatments in atopic dermatitis. *Dermatol Open J.* 2017; 2(2): e3-e4. doi: 10.17140/DRMTOJ-2-e003

Emerging Age of Opportunity for More Effective Treatments in Atopic Dermatitis

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Atopic dermatitis (AD) is a chronic inflammatory disease characterized by widespread lesions, which manifest as erythematous areas with crusting and/or scaling, oozing, excoriations, and lichenification. Additionally, pruritus/itching is one of the major symptoms of the disease which has prompted a description of AD as "the itch that rashes". Combined, these symptoms significantly impact on the quality of life (QoL) for millions of individuals worldwide. For years, AD was primarily considered a disease that affected children and adolescents, but recent epidemiological studies have highlighted the increased incidence of disease among the adult population as well.

Until recently, individuals with AD had very few options for effective treatment of their disease. Individuals were predominantly managed through the use of topically applied steroids, calcineurin inhibitors (i.e., pimecrolimus, tacrolimus), or immunosuppressive agents (i.e., cyclosporine, mycophenolate mofetil) to suppress the inflammatory response and restore skin barrier function; allergen avoidance to prevent disease exacerbation and acute flares; and antimicrobial agents to prevent secondary skin infections. In severe cases, patients received oral antihistamines and anti-anxiety medications to alleviate the insatiable itching. These treatments are relatively effective in individuals with more mild disease, but the treatment effect is short-lived and does not provide long-term relief or remission for the more moderate to severe patients. Additionally, long-term use of steroids may be associated with significant side effects which subsequently increases the anxiety of patients and may reduce patient compliance.

Recent advances in our understanding of AD have further illustrated the complex nature of the disease. Specifically, research has demonstrated that AD is a complex interaction of barrier disruption and systemic inflammation which drives disease pathogenesis. For years, it was believed that T-helper 2 (Th2)-mediated inflammation in the skin was the predominant culprit for the disruption of the skin barrier and increased risk of skin infections. Additionally, the increased Th2 signaling was responsible for the increased pruritus observed in these patients as well. More recently, genomic and proteomic approaches have shown that AD patients are more heterogeneous that initially thought. This heterogeneity has prompted further characterization of the different inflammatory axes and the corresponding subsets of AD patients. As a result of these investigations, it's now known that AD patients can have elevated Th2 inflammation as well as increased T-helper 22 (Th22)- and T-helper 17 (Th17)-mediated inflammation.

Corresponding with our increased understanding of the inflammatory axes in AD, there has been an increase in novel therapeutic approaches targeting these specific inflammatory pathways. A monoclonal antibody targeting interleukin-4 receptor alpha (IL-4Rα; dupilumab) was recently approved for the treatment of moderate to severe AD and additional monoclonal antibodies targeting IL-13, thymic stromal lymphopoietin (TSLP), IL-33, and OX-40 are currently in clinical trials as well. Similarly, crisaborale, a topical ointment that targets phosphodiesterase 4 (PDE4), was approved for the treatment of mild to moderate AD. Additional therapies are currently in clinical trials evaluating the effects of janus kinase (JAK), aryl hydrocarbon receptor (AHR), and chemoattractant receptor-homologous molecule expressed on T-helper 2 cells (CRTH2) antagonists in various severities of AD.

As our understanding of AD continues to increase, we deviate from the idea that AD is

ISSN 2473-4799 http://dx.doi.org/10.17140/DRMTOJ-2-e003

a cosmetic disease with severe itching to a more appropriate acceptance that AD is a systemic autoimmune disease with significant skin inflammation. As such, the emergence of new therapeutic options provides the hope that resolution and remission may soon be a reality for the millions of patients suffering from AD.

ACKNOWLEDGMENTS

The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the Incyte Corporation.