Historically, alopecia areata and atopic dermatitis have been considered to be two separate diseases with different etiologies and pathogenesis. But as more knowledge is gained regarding genetics and biological pathways, some overlap has been found between the two diseases.

In February, NAAF and the International Eczema Council (IEC) hosted a joint symposium during the 77th Annual American Academy of Dermatology meeting in Washington, DC, to explore the similarities and differences between these two common but complex skin diseases and the implications from bench to bedside. The meeting, Atopic Dermatitis and Alopecia Areata: Comparison and Contrast, received an enthusiastic response with an audience of more than 250 participants, including 138 biopharmaceutical industry representatives from 24 different companies.

Our symposium Chairs, Drs. Emma Guttman and Natasha Mesinkovska, designed a program focused on the epidemiology, comorbidities, pathogenesis, therapeutic advances, and patient perspectives on clinical trials and treatments for alopecia areata and atopic dermatitis, highlighting overlap and differences between the two.

### Epidemiology and Comorbidities

Dr. Aaron Drucker, from Women’s College Hospital and the University of Toronto (Toronto, Canada), shared data from large epidemiologic studies showing atopic dermatitis is associated with a significantly increased risk of developing alopecia areata. Potential explanations for the observed association include shared genetic risk loci and also common environmental triggers as well as detection bias. Further studies should include larger populations of children, people with different ethnic backgrounds, and validated case definitions. Future high-quality studies may also help elucidate the impact of comorbid atopic dermatitis and alopecia areata on severity and prognosis.

Dr. Natasha Mesinkovska, NAAF’s Chief Scientific Officer and Director of Clinical Research at the University of California Irvine School of Medicine (Irvine, CA), presented increasing evidence that cardiovascular disease, neuropsychiatric disease, and infections are comorbidities of atopic dermatitis in addition to the well-established atopic conditions. Comorbidities of alopecia areata include thyroid disease, other autoimmune diseases, atopic conditions, nutritional deficiencies, and audiologic and ophthalmic abnormalities. Physicians should be aware of these potential comorbid conditions and consider them when choosing therapy. Further studies are needed to evaluate the significance and causality of these associations and whether treatment can help with prevention of certain comorbidities.

### Pathogenesis

Dr. Emma Guttman, from the Icahn School of Medicine at Mount Sinai (New York, NY), presented the latest developments in understanding the complex multifactorial pathogenesis of atopic dermatitis, particularly the recognition of its systemic nature and the central role of type 2 cytokine activation, such as IL-4, IL-13, and IL-31. Contributions of these pathways are confirmed by the excellent response of atopic dermatitis to dupilumab, establishing the Th2 immune axis as central to the pathogenesis of disease and the need for systemic treatment approaches. Applying narrow-targeted therapeutics aimed at specific cytokine inhibition has helped dissect the pathogenic contributions of key immune pathways in atopic dermatitis, and similar clinical trials with targeted therapeutics against different axes may help elucidate the role of each cytokine pathway in the development of alopecia areata.

Dr. Ralf Paus, from the University of Miami (Miami, FL) and the University of Manchester (Manchester, UK), discussed the genetics, environmental factors and immune response mechanisms that result in alopecia areata. The disease manifests when the immune privilege of the hair follicles is impaired and immune cells infiltrate around the hair bulb during the anagen phase, causing hair follicle dystrophy and premature catagen induction. Immunogenetic studies have specifically implicated the interferon
gamma pathway and its related cytokines as well as a predominant signature for cytotoxic T cells as central to the pathogenesis of alopecia areata, and new therapeutic approaches are focused on inhibition of autoimmunity. But alopecia areata may be better viewed as a stereotypic hair follicle response pattern to interferon gamma immunological damage, and a deeper understanding of the mechanisms that jointly maintain hair follicle immune privilege is needed for more effective patient-specific therapies.

Therapeutic Advances

Dr. Eric Simpson, from Oregon Health & Sciences University (Portland, OR), presented on the therapeutic landscape in atopic dermatitis as more knowledge is gained about the immunopathogenesis and more targeted therapies are being developed for atopic dermatitis. The first-in-human topical microbial translocation with Roseomonas mucosa for atopic dermatitis showed efficacy and could lead to prevention. Biologics aimed at inhibiting IL-4 and IL-13 cytokines have been shown to be effective and safe therapeutic strategies in atopic dermatitis. Blockade of other extracellular targets such as IL-31, IL-33, IL-17 appear to have utility in atopic dermatitis. Oral and topical JAK inhibitors in various stages of clinical development represent another promising treatment option, but efficacy will need careful balancing with side effect profiles.

Dr. Brett King, from the Yale School of Medicine (New Haven, CT), discussed therapeutic advances in alopecia areata. Genetic and preclinical studies revealed the JAK-STAT signaling pathway as a major pathogenic driver of alopecia areata, which provided the rationale for investigation of JAK inhibitors. There have been many clinical studies of JAK inhibitor efficacy in alopecia areata using both oral and topical formulations. Other therapeutic possibilities being evaluated for their utility in alopecia areata include apremilast, an oral phosphodiesterase-4 inhibitor; ustekinumab, an IL-12/23 inhibitor; dupilumab, IL-4/13 inhibitor; and fecal microbiota transplants.

Dr. Amy Paller, from Northwestern University Feinberg School of Medicine (Chicago, IL), and Dr. Leslie Castelo-Soccio, from the University of Pennsylvania School of Medicine and Children’s Hospital of Philadelphia (Philadelphia, PA), presented jointly on atopic dermatitis and alopecia areata in the pediatric population. Both diseases can have different features than in adults, including clinical features, disease course and tolerance to therapy. Ninety percent of atopic dermatitis patients are younger than age 5 when diagnosed and 40 percent of alopecia areata patients experience their first episode before age 20. Children with atopic dermatitis and alopecia areata experience poorer quality of life, including higher rates of anxiety and depression. There are several treatment options common to pediatric atopic dermatitis and alopecia areata, and emerging therapies that may be effective for both, including topical and oral JAK inhibitors.

Outcome Measures

Dr. Jonathan Silverberg, from Northwestern University Feinberg School of Medicine (Chicago, IL), presented on outcome measures for atopic dermatitis and how this can be implemented in alopecia areata. The Harmonizing Outcome Measures for Eczema (HOME) initiative was established to develop a consensus-based core outcome set for clinical trials and clinical practice. The Eczema Area and Severity Index (EASI) instrument for clinician-reported signs and the Patient-Oriented Eczema Measure (POEM) tool for measuring patient-reported symptoms are recommended by the HOME initiative as the core outcome instrument in atopic dermatitis trials. Work is ongoing to identify suitable instruments for quality of life. More validation studies are needed for alopecia areata outcome measures, including the Severity of Alopecia Tool (SALT) and Alopecia Density and Extent (ALODEX) score.

Patient Perspective on Clinical Trials

A panel of three patient advocates was convened to share their experiences participating in clinical trials, including their individual motivations, challenges and outcomes. They provided valuable insights to help all stakeholders work together to improve future clinical trials that align with patient’s needs and preferences.

A common theme of the discussion was centered on the need to provide a pathway for participants to access support and other resources to minimize burden and improve recruitment and retention. The main recommendations for those running clinical trials were: 1) refer participants to patient advocacy organizations like NAAF and the National Eczema Association (NEA) for support, information, useful resources and to connect with other patients; and 2) have experienced study participants serve as patient ambassadors to bring information about trials to their social networks and communities.

Concluding Remarks

This joint symposium highlighted recent advances in atopic dermatitis and alopecia areata research, providing insight into their similarities and differences from genetics to immunology to therapeutic development. Continued collaborative research will help researchers and clinicians better understand the complex pathophysiology of these two diseases, develop new targeted treatments, and improve the overall care of patients.