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 ORIGINAL ARTICLE

A Consensus on *Staphylococcus Aureus* Exacerbated Atopic Dermatitis and the Need for a Novel Treatment

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ABSTRACT

The skin microbiome is essential for skin barrier function because it inhibits pathogen colonization, and decreased microbiome diversity correlates with increased *Staphylococcus aureus* (*S. aureus*) burden and atopic dermatitis (AD) severity. Managing *S. aureus*-driven AD in clinical practice remains problematic due to complications such as AD exacerbation, impetigo, abscesses, and invasive infections. This project used a modified Delphi process comprising face-to-face discussions followed by a blinded vote to define 5 final consensus statements. A panel of 6 pediatric dermatologists developed a consensus on *S. aureus*-driven AD exacerbation, challenges in current treatments for AD with secondary bacterial infections, and new developments to improve patient care and outcomes. The panel's 5 consensus statements provide recommendations for dermatologists, pediatricians, and healthcare providers treating patients with secondary infected AD. These recommendations underscore the importance of recognizing and managing *S. aureus* skin infection in AD clinical practice and promoting antibiotic stewardship to mitigate resistance. The panel defined a significant unmet need for a single topical AD therapy effective against all symptoms, including pruritus, *S. aureus*-driven AD exacerbation, infection, and inflammation, across AD severity levels.

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INTRODUCTION

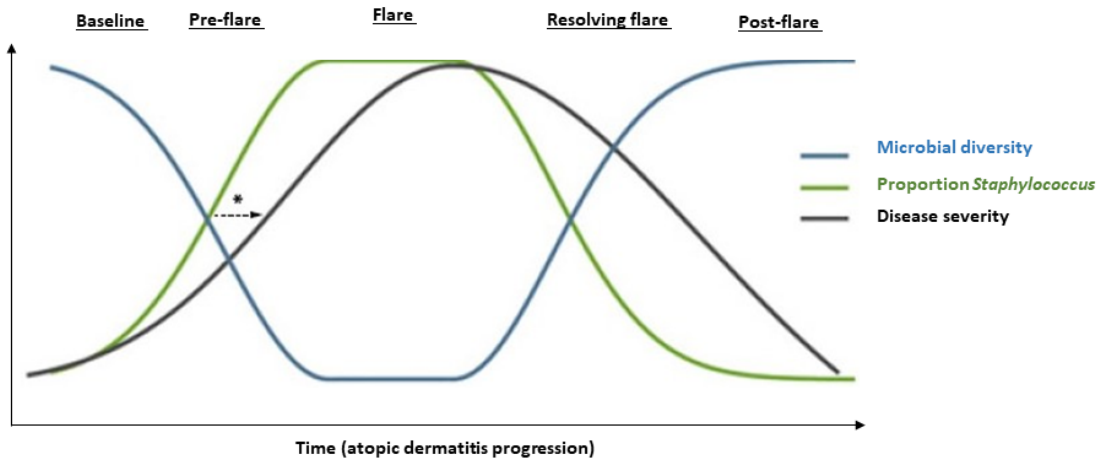
Current Clinical Challenges in Atopic Dermatitis Management and Treatment

Despite advances in topical and systemic treatment options for atopic dermatitis (AD), challenges persist in effectively managing the condition, leading to significant disruption to patients and their families.[1] AD has the highest global burden among skin disorders, and hospitalizations due to AD flares and related infections are associated with an 8.3-year reduction in lifespan.[2-4] In addition, over 60% of adults report severe or unbearable pruritus, and 55% of adults with moderate-to-severe AD experience inadequate disease control.[5-7] AD outpatient visits have increased to almost 2 million annually. Dermatologist visits are more frequent for chronic AD, and primary care physician visits are more frequent for acute AD, particularly in pediatric patients under 4 years old.[1,8] This highlights the need for improved AD treatment and disease control, especially in pediatric patients, and for the ongoing education of all pediatric healthcare providers.

The skin microbiome is essential for skin barrier function, inhibiting pathogen colonization and modulating immune responses.[9,10] The microbiome contributes to immune system development in infants and AD occurrence.[9,10] Furthermore, reduced microbiome diversity correlates with increased *Staphylococcus aureus* (*S. aureus*) burden and AD disease severity.[1,10]

S. aureus plays a central role in AD exacerbation, skin colonization, and infectious complications, and managing *S. aureus*-driven AD remains problematic. Evidence shows that *S. aureus* is increased with higher AD severity and is associated with infectious complications such as impetigo, cellulitis, abscesses, and invasive infections.[11-14] Up to 90% of patients with AD are colonized with *S. aureus*, often both in lesional and nonlesional skin.[15,16] Furthermore, increased *S. aureus* colonization is linked to microbial dysbiosis and reduction of skin microbiome diversity.[10] Indeed, decreased skin microbiome diversity and increased *S. aureus*

FIGURE 1. *Staphylococcus aureus* role in skin microbial diversity and atopic dermatitis exacerbation.[10]



AD microbiome progression hypothesis. (*) Proposed relationship among shifts in skin microbial diversity, the proportion of *S. aureus*, and disease severity.

abundance were observed during AD flares (see Figure 1).[10] *S. aureus* colonization precedes AD onset in children, suggesting a causative role in AD flares and AD exacerbation.[11,17]

Secondary bacterial infection due to *S. aureus* skin colonization, particularly methicillin-resistant *S. aureus* (MRSA), poses a challenge in AD treatment. *S. aureus* isolates from patients with AD show MRSA prevalence ranging from 10% to 30%.[11,18-20] MRSA colonization is significantly associated with antibiotic misuse and previous hospitalization.[12,20,21]

A New Atopic Dermatitis Therapeutic That Treats Pruritus, Bacterial and Immune Components

Therapies for AD may target pruritus, *S. aureus*-driven AD exacerbation, secondary bacterial infection, inflammation, xerosis, and reduced skin barrier function. Topical or systemic antibiotics are sometimes used to treat *S. aureus* infection in patients with AD, with systemic antibiotics typically used for MRSA control.[22-24] The botanical drug zabalafin 40% hydrogel (AB-101a, Alphyn) offers a promising alternative to anti-inflammatory and antibiotic drugs in treating *S. aureus*-driven AD and related symptoms.[25] Zabalafin represents a first-in-class multi-target therapeutic topical drug with multiple mechanisms of action, including anti-pruritic, antibacterial, and anti-inflammatory activity.[25] Zabalafin addresses the unmet need for a single topical AD therapy suitable for patients with pruritus and secondary bacterial infection without systemic side effects.

MATERIALS AND METHODS

The project used a modified Delphi process comprising face-to-face expert panel discussions and follow-up.

Literature Review

Systematic literature searches of English-language literature on *S. aureus*-infected pediatric impetiginized AD and impetigo/skin and soft tissue infection (SSTI) were performed on June 17 and 18, 2023, using PubMed and Google Scholar as secondary sources (Table 1). The searches encompassed clinical trials, research studies, clinical guidelines, consensus papers, and reviews providing original data published between January 2010 and May 2023 (Table 2). Articles without original data, pediatric patients with AD/impetigo, or publications in languages other than English were excluded (Figure 2).

TABLE 1.

Systematic Literature Review Search Terms		
Group 1: AD and *Sa* infection	**Group 2: Impetiginized AD**	**Group 3: Impetigo**
Pediatric/childhood AD* AND *Sa* infection**OR impetiginized OR prevalence impetiginized OR skin commensal bacteria OR **acute OR **chronic OR severity and *Sa* infection** OR skin dysbiosis OR epidermal barrier dysfunction OR *Sa*-related filaggrin breakdown products OR Sa-related risk for invasive infection OR MRSA	**AND antimicrobial resistance OR antimicrobial susceptibility OR bleach baths OR topical antimicrobial	Impetigo/SSTI*** AND antimicrobial resistance OR mupirocin resistance OR MRSA OR fusidic acid OR retapamulin OR topical ozenoxacin OR chlorhexidine OR levofloxacin OR ciprofloxacin

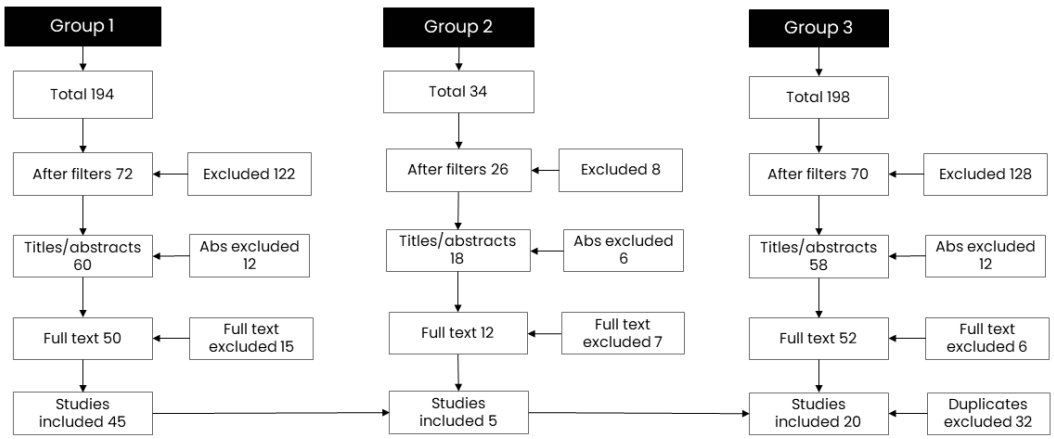
AD, atopic dermatitis; MRSA, methicillin-resistant *Sa; Sa, Staphylococcus aureus*; SSTI, skin and soft tissue infection.

TABLE 2.

Selected Pediatric Atopic Dermatitis and Impetigo/Skin and Soft Tissue Articles		
No	**Reference**	**Subject**
1	McNeil JC et al. *Antimicrob Agents Chemo.* 2011	Mupirocin resistance in *S. aureus* causing recurrent skin and soft tissue infections in children.
2	Leifso KR et al. *Can J Infect Dis Med Microbiol.* 2013	Clinical characteristics of pediatric patients hospitalized with methicillin-resistant *S. aureus.*
3	McNeil JC et al. *Antimicrob Agents Chemo.* 2014	Decreased susceptibilities to retapamulin, mupirocin, and chlorhexidine among *S. aureus* isolates.
4	Rørtveit S et al. *Scand J Infect Dis.* 2014	Fusidic acid-resistant impetigo.
5	Van Bijnen EM et al. *BMC Fam Pract.* 2014	Primary care treatment guidelines for antimicrobial resistance found in commensal *S. aureus* skin infections.
6	Chaturvedi P et al. *N Am J Med Sci.* 2014	Mupirocin-resistant *S. aureus.*
7	Gropper S et al. *Future Microbiol.* 2014	Ozenoxacin 1% cream for impetigo: a multicenter, randomized, placebo- and retapamulin-controlled clinical trial.
8	Antonov NK et al. *Antimicrob Agents Chemo.* 2015	High prevalence of mupirocin resistance in *S. aureus* isolates from a pediatric population.
9	Rezende et al. *An Bras Dermatol.* 2016	*S. aureus* resistance to topical antimicrobials in atopic dermatitis.
10	Doudoulakakis A et al. *J Clin Microbiol.* 2017	*S. aureus* clone resistant to mupirocin and fusidic acid carrying exotoxin genes and causing mainly skin infections.
11	Williamson DA et al. *Clin Microbiol Rev.* 2017	Current and emerging topical antibacterials and antiseptics: agents, action, and resistance patterns.
12	Harkins CP et al. *Br J Dermatol.* 2018	Widespread use of topical antimicrobials enriches for resistance in *S. aureus* isolated from patients with atopic dermatitis.
13	Rosen T et al. *JAMA Dermatol.* 2018	Efficacy and safety of ozenoxacin cream for adult and pediatric patients with impetigo: a randomized clinical trial.
14	Canton R et al. *Future Microbiol.* 2018	Comparative in vitro antibacterial activity of ozenoxacin against Gram-positive clinical isolates.
15	Herbert AA et al. *Drugs Dermatol.* 2018	Topical antibacterial agent for treatment of adult and pediatric patients with impetigo: pooled analysis of phase 3 clinical trials.
16	Shi B et al. *J Invest Dermatol.* 2018	Methicillin-resistant Staphylococcus aureus colonization is associated with decreased skin commensal bacteria in atopic dermatitis.
17	López Y et al. *Plos One.* 2019	Mutant prevention concentration of ozenoxacin for quinolone-susceptible or -resistant *S. aureus* and *S. epidermidis.*
18	Koulenti D et al. *Microorganisms.* 2019	Novel antibiotics for multidrug-resistant gram-positive microorganisms.
19	Anusha Rani MV et al. *Natl J Physiol Pharma Pharmacol.* 2019	Comparison of efficacy and cost-effectiveness of topical fusidic acid and topical mupirocin for impetigo
20	Vila J et al. *Expert Rev Anti Infect Ther.* 2019	Ozenoxacin: a review of preclinical and clinical efficacy.
21	Wang V et al. *Ann Allergy Asthma Immunol.* 2019	Antibiotic choice and methicillin-resistant *S. aureus* rate in children hospitalized for AD.
22	López Y et al. *Int J Antimicrob Agents.* 2020	Comparative activity of ozenoxacin and other quinolones in *S. aureus* strains overexpressing the efflux pump-encoding genes mepA and norA.

AD, atopic dermatitis; *S. aureus, Staphylococcus aureus.*

FIGURE 2. Results of the systematic literature searches.



After applying search filters and excluding duplicates 70 articles were selected.
Excluded: No original data, publication language other than English, not including pediatric patients with AD or impetigo.
Included: N = 70.

Role of the Panel

An expert panel (N = 6) of pediatric dermatologists convened on July 3, 2023, to provide insights into *S. aureus*-driven AD exacerbation, challenges of current secondary bacterial infection AD treatments, and new developments to improve patient care and outcomes. The panel developed 5 consensus statements from the selected literature. The panel evaluated the draft statements and supporting literature using literature evidence coupled with their opinions and experiences. Panel consensus was established through blinded votes to define the final statements.

RESULTS

Consensus Statements

The expert panel was tasked with choosing 5 top statements to describe the importance of treating *S. aureus*-driven AD exacerbation and secondary bacterial infection in AD. The panel reached a consensus (6/6) on the 5 statements discussed in this paper.

Statement 1: *Currently, no single product is effective against all signs and symptoms of (AD), including xerosis, pruritus, infection, and S. aureus-driven AD exacerbation.*

Treatment of secondary infected AD often includes topical or oral antibiotic therapy. However, antimicrobial resistance is a global concern that must be considered when selecting AD treatment.[26,27] Topical therapy of infected eczema is recommended for patients with limited skin involvement, whereas oral antibiotics are used for patients with severe secondary infected.[24,28] However, no single antibiotic is appropriate for all secondary infected AD severities and effective against all *S. aureus* strains, and consideration of antibiotic resistance is essential.[24,26] Resistance to mupirocin has been increasing in AD patients with Staph colonization and infection.

Ozenoxacin belongs to a new class of non-fluorinated quinolones for topical secondary infected AD treatment and is highly effective against *S. aureus*, including MRSA. The ozenoxacin mutant prevention concentration for *S. aureus* and MRSA was significantly below epidermis ozenoxacin levels, making resistance unlikely.[29] Several clinical studies showed that ozenoxacin was superior to retapamulin or placebo in microbiological clearance and impetigo treatment in pediatric and adult patients.[30,31,32] Thus, ozenoxacin is effective in treating impetigo caused by *S. aureus*, including MRSA.[29,33]

Nevertheless, long-term secondary infected AD antibiotic therapy has limitations due to the increasing antibiotic resistance and a negative impact on the cutaneous microbiome.[34,18,35] Topical antibiotic therapy has had limited success in reducing AD severity caused by resistant *S. aureus* and MRSA colonization.[18,36] Alternative strategies to manage *S. aureus*, including MRSA colonization, may be helpful for effective secondary bacterial-infected AD treatment.[18,35]

Alternatives to long-term antibiotic therapy include dilute bleach baths, topical microbiome transplantation, or *S. aureus* targeting phage endolysin.[37] Several clinical studies reported that dilute bleach baths improve secondary infected AD symptoms and severity as well as restore skin microbiome by eradicating pathogens, including *S. aureus*.[22,38] However, a recent meta-analysis showed no additional bleach bath benefits compared with water bath alone.[23] Furthermore, several studies have shown bleach baths do not address *S. aureus*-driven AD.[39,40]

Results on topical epidermal microbiome transplantation with *S. hominis* and *S. epidermidis* or *Roseomonas mucosa* for AD vary; phase 2 clinical studies showed negative results.[41,42]

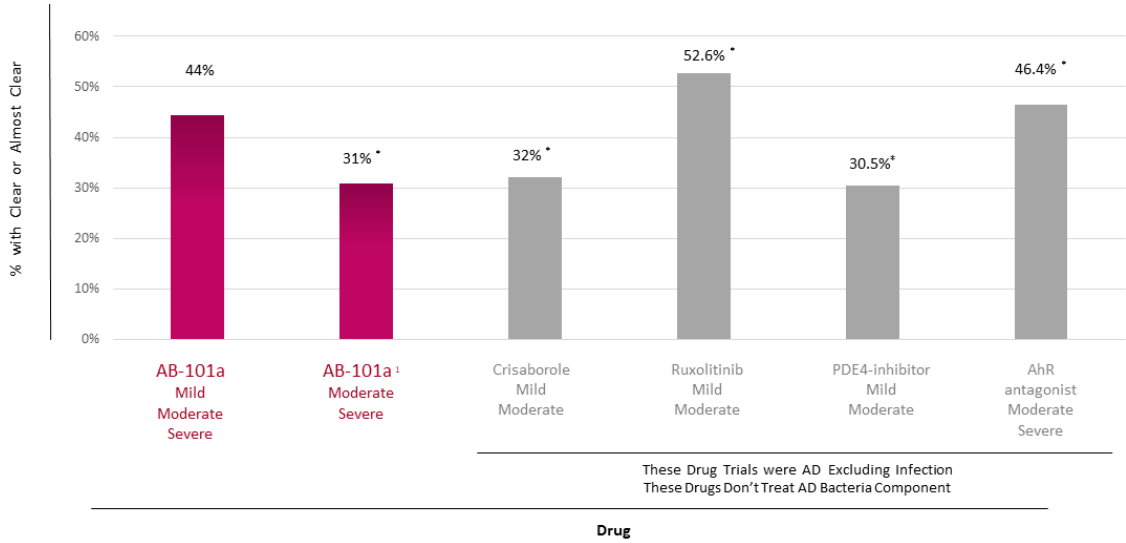
Zabalafin is a first-in-class secondary infected/secondary bacterial-infected AD treatment with multiple mechanisms of action, including anti-pruritic, antibacterial, and anti-inflammatory activity.[25] A Phase 2a clinical trial evaluated zabalafin efficacy in 37 pediatric and adult patients with non-infected AD (19 patients) and AD with secondary bacterial infection (18 patients).[25] Interim results in the secondary infected patient cohort show zabalafin controlled the AD bacterial component with 84% of infections cleared and 44% of patients achieved AD symptom clear or almost clear (see Figure 3). Zabalafin was comparably effective in the non-infected AD cohort. Thus, zabalafin addresses the unmet need for a single topical AD therapy that treats all AD severities and symptoms including pruritus, secondary bacterial infection, inflammation, and *S. aureus*-driven AD exacerbation.

Statement 2: *S. aureus almost universally colonizes the skin of AD patients, contributing to AD infections and the development of flares and exacerbations.*

S. aureus commonly colonizes the skin of patients with AD and contributes to AD development, flares, and exacerbation. Up to 90% of AD patients are colonized with *S. aureus*, often both in lesional and nonlesional skin.[15,16,43,44] More severe AD is associated with greater predominance of *S. aureus* colonization.[13,43,44] Importantly, *S. aureus* colonization precedes AD onset in children, and evidence shows *S. aureus* contributes to AD development, flares, and exacerbation in children and infancy.[11,17,45] Multiple risk factors are associated with *S. aureus* colonization: *S. aureus*-corneocyte adhesion strength, antimicrobial peptide deficiency, decreased levels of filaggrin, and filaggrin degradation products; overexpressed Th2/Th17 cytokines; altered lipid profiles; and microbial dysbiosis.[11,16,41,46-53]

Increased *S. aureus* colonization is associated with microbial dysbiosis and reduction of skin microbiome diversity.[10,54] Indeed,

FIGURE 3. Interim Investigator's Global Assessment results of Phase 2a clinical trial evaluating zabalafin (AB-101a) efficacy in 19 pediatric and adult patients with atopic dermatitis and secondary bacterial infection.[25]

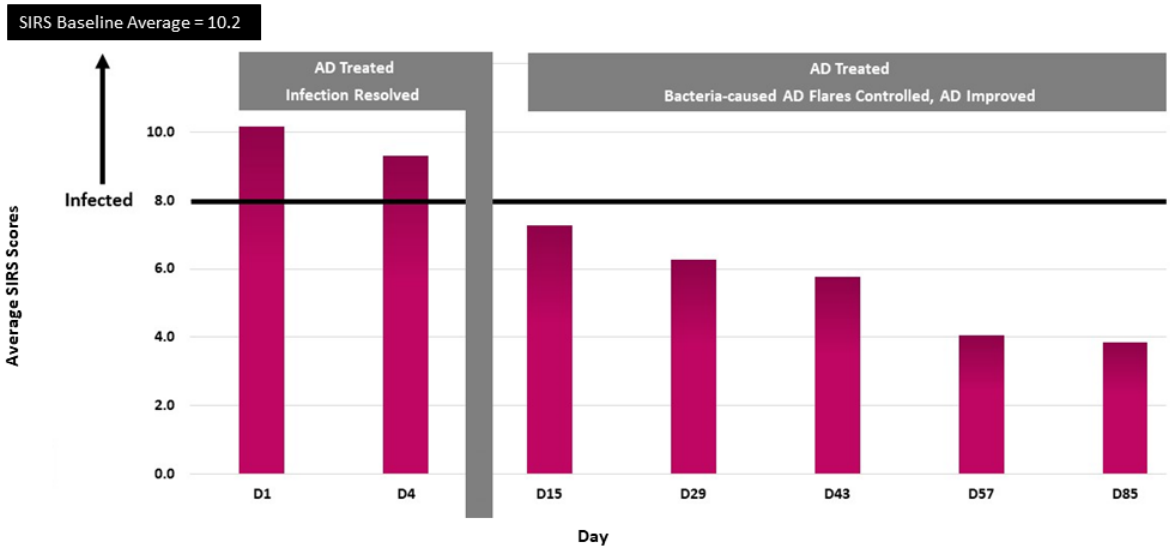


*IGA final of clear (0) or almost clear (1) with >2 improvement in IGA from baseline.
AB-101a clinical trial included AD patients with a secondary infection. The other trials excluded AD patients with a secondary infection.

decreased skin microbiome diversity and increased *S. aureus* abundance were observed during AD flares (see Figure 1).[10] *S. aureus* colonization on AD skin causes microbial dysbiosis and skin barrier dysfunction through virulence factors such as toxins, enzymes, and other proteins.[46,49,55] Several clinical studies have shown microbiome restoration using prebiotic emollients containing *V. filiformis* lysate or endolysin reduces *S. aureus* abundance, normalizing skin microbiome and decreasing AD symptoms and severity.[35]

Increased *S. aureus* abundance and decreased skin microbiome diversity precede and cause AD flares and exacerbation.[10] Untreated AD flares have more *S. aureus* and less microbiome diversity than intermittent and post-treatment flares.[10,56] Furthermore, lack of AD flare treatment leads to vicious cycles between *S. aureus* colonization and AD exacerbation.[10,56] Based on these results, consistent AD treatment over a period of time is required to reduce *S. aureus* colonization and restore microbiome diversity.

FIGURE 4. Interim systemic inflammatory response syndrome results of Phase 2a clinical trial evaluating zabalafin (AB-101a) efficacy in 19 pediatric and adult patients with atopic dermatitis and secondary bacterial infection.[25]



Assessment of skin infection (rating pruritus, inflammation, blistering, exudate, and crusting) showed a correlation with physician assessment of infection and scores on other AD measurement scales (IGA, EASI), indicating that zabalafin is effective in controlling bacteria-driven AD flares.

The Phase 2a study of zabalafin in AD patients assessing skin infection (rating pruritus, inflammation, blistering, exudate, and crusting) showed a correlation with physician assessment of infection and scores on other AD measurement scales (Investigator's Global Assessment [IGA], Eczema Area and Severity Index [EASI]), indicating that zabalafin is effective in controlling bacteria-driven AD flares (see Figure 4).

Statement 3: *Methicillin-resistance and mupirocin resistance by S. aureus are associated with decreased skin commensal bacteria and an increased risk of secondary infection.*

The MRSA prevalence in patients with AD is increasing, with up to 30% of patients being MRSA positive.[11,18-20] Furthermore, microbial diversity and composition are further decreased in MRSA-colonized AD skin compared with methicillin-sensitive *S. aureus* (MSSA)-colonized AD skin.[18] This leads to more severe AD inflammation in patients with MRSA compared with AD skin in patients with MSSA.[11]

MRSA-driven infection poses a major challenge in AD treatment due to the increased risk associated with MRSA invasive infections.[11,12] MRSA causes increased AD severity and inflammation associated with reduced skin barrier integrity and increases the risk for invasive MRSA infection.[11,57,58] Indeed, AD-associated invasive infections show a higher rate of MRSA.[12] Furthermore, antibiotic resistance is increasing in AD and SSTI-associated MRSA, complicating invasive MRSA antibiotic treatment and increasing the systemic MRSA infection risks.[19,20,59-61] In addition to topical antibiotic resistance, SSTI-associated MRSA shows increased epidermolysis, which causes impetigo.[57,62]

Statement 4*: Stewardship in topical and systemic antibiotics is warranted.*

Widely reported *S. aureus* resistance to topical and oral antibiotics for impetiginized AD treatment necessitates antibiotic stewardship.[26] Specifically, resistance to commonly used antibiotics, including fusidic acid, mupirocin, clindamycin, retapamulin, chlorhexidine, neomycin, and bacitracin, is increasing in AD and SSTI-associated MRSA.[19,20,59-61] Furthermore, resistance correlates with the most used antibiotics in each region, suggesting antibiotic overuse and emphasizing the need for topical antibiotic stewardship.[26,63,64]

However, antimicrobial stewardship guidelines mainly focus on oral or intravenous antibiotics, and few studies quantify the extent of topical antibiotic use or assess prescribing practices.[26,65,66] Yet, topical antibiotics are among the most commonly prescribed antimicrobial treatments.[26,66] Clinical guidelines on topical antibiotic treatment of *S. aureus*-driven SSTIs mostly recommend fusidic acid and mupirocin despite reported widespread resistance.[65,24] Stewardship is essential to preserve the efficacy of emerging topical antimicrobials such as ozenoxacin.[33] Recommended approaches to topical antibiotic stewardship include a global action plan focused on resistance awareness.[26,66,67] Improved evidence-based clinical guidelines and continued education on topical antibiotics in AD treatment will enable the implementation of best practices for topical antibiotic stewardship and slow resistance rates.[26,65,66]

Zabalafin combines bioactivity with multiple mechanisms against bacteria, reducing concerns for developing drug resistance, and may fit the equipment for antibiotic stewardship in treating impetiginized AD.

Statement 5: *A needed and effective treatment for AD may have the following features:*

a. Long-term safety profile enabling long-term continuous use in children down to age 2 years and preferably younger and in all anatomic areas.
b. Effective against the bacterial component of AD, which includes effective treatment of AD with secondary bacterial infection and effective controlling the bacterial microbiome on the AD skin to attenuate AD future flares.

AD poses a large unmet need for a single topical AD therapy effective against all AD severities and symptoms, including xerosis, pruritus, secondary bacterial infection, inflammation, and *S. aureus*-driven AD exacerbation.[34,68] Despite emerging alternative antimicrobial treatments becoming available, antibiotic therapy remains a core part of treatment for secondary bacterial infected AD in clinical practice.[24,67] However, widespread and increasing antibiotic resistance to current treatments limits their use and future efficacy.[24,26] Effective topical AD treatment should include skin barrier restoration and protection, reduce *S. aureus*-driven infection, control inflammation and flares, including *S. aureus*-driven AD flares, and eliminate pruritus and xerosis.[68]

AD prevalence is highest in early childhood; hence, appropriate AD treatment must be effective and safe for long-term continuous use in children and infants.[2,8] As *S. aureus* colonization often precedes AD onset and contributes to AD development and exacerbation in children and infants as well as adults, effective AD treatment in children and adults must address *S. aureus*-driven impetigo and AD exacerbation.[11,17,45]

Reducing *S. aureus* colonization and restoring microbiome diversity and skin barrier function is essential to resolve AD flares and chronic disease.[10,56] Preventative treatment to restore the skin barrier and reduce *S. aureus* colonization leads to improved microbiome diversity.[10,35,41,68,69] Furthermore, since current AD therapies are not curative, such preventative AD treatment may improve long-term outcomes.[68,69] Further clinical research directly comparing topical antimicrobials in secondary infected AD treatment is needed, particularly in high-resistance settings.[69]

DISCUSSION

AD presents a significant unmet need for a single topical AD therapy effective against all AD signs and symptoms in both pediatric and adult patients.[34,68] Despite widespread antibiotic resistance and emerging alternative antimicrobial treatments, antibiotics remain the first-line treatment for secondary bacterial-infected AD in clinical practice.[24,26,67] The panel noted that zabalafin is an anti-inflammatory with broad-spectrum antibacterial properties, not an antibiotic. Pruritus is a significant burden in patients with AD, and pruritus treatment is essential in effective AD management.[7] Zabalafin presents a first-in-class anti-pruritus treatment. Zabalafin may address the unmet need for a single topical AD therapy that treats pruritic and bacterial components.

According to some panelists, assessing redness and inflammation signs used in The European Task Force on AD, which recommends SCORAD as a rating tool, might introduce outcome measures for studying AD and the microbiome's influence.[70]

Additionally, the panel recommends that assessing skin microbiome normalization in AD assessment and rating to investigate microbial diversity in AD patients compared with controls before and after treatment may be useful. Decreased skin microbiome diversity and increased *S. aureus* abundance are observed during AD flares, and flare resolution is associated with increased microbiome diversity and decreased *S. aureus* colonization.[10] Thus, microbiome normalization indicates AD treatment efficacy and correlates with decreased *S. aureus* infection.

S. aureus skin colonization, particularly MRSA, remains a major challenge in AD management and treatment.[10,11] The panel recommends that dermatologists and pediatricians incorporate the management of *S. aureus* on the skin into AD clinical practice for both skin infection and in consideration of *S. aureus*-driven AD when stable patients with AD experience flaring. The panel also recommends providing all patients with AD with an instructional handout outlining a therapeutic ladder to enhance patient engagement with AD treatment and adherence.[71]

Limitations

AD is a complex condition with a multitude of contributing genetic and environmental factors. This manuscript focuses primarily on *S. aureus*-driven AD and is not intended to fully encompass all AD aspects, including genetic, environmental, and other microbial factors. The literature review for this manuscript focused on articles published between January 2010 and May 2023. This limited timeframe may not capture the most recent research and developments in the field of *S. aureus*-driven AD treatment and management. The systematic literature search was limited to English-language literature. This potentially excluded relevant research published in other languages, such as region-specific studies that are critical for understanding the prevalence and management of *S. aureus* in different geographic areas.

CONCLUSION

Effective AD therapy should include topical treatment that restores the skin barrier, reduces *S. aureus*-driven secondary bacterial infection, controls inflammation and flares, including *S. aureus*-driven AD flares, and eliminates pruritus and xerosis. With its anti-pruritic and antibacterial properties, the emerging agent, zabalafin, may address an unmet need for a single topical therapy that treats all AD symptoms and severities in pediatric and adult patients. However, further clinical research and guideline amendments are needed to change antibiotics as first-line treatment for secondary infected AD in clinical practice. Antibiotic stewardship in secondary bacterial infection AD treatment is essential to prevent widespread and increasing antibiotic resistance. Clinician education is needed to improve knowledge of effective secondary bacterial infection AD therapy strategies and strategies for effective therapy to prevent *S. aureus*-driven AD exacerbation, considering the role of *S. aureus*, including MRSA and the skin microbiome.

DISCLOSURES

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