Atopic Dermatitis

A supplement to Dermatology News - November 2021

PATIENT SATISFACTION WITH TREATMENT

REDUCING ITCH

BURDEN OF DISEASE IN BLACK PATIENTS

BATHING RECOMMENDATIONS

Commentary by
Zelma C. Chiesa Fuxench, MD, MSCE

ITCH-SCRATCH-
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ITCH-SCRATCH-

THE ONE-OF-A-KIND
TOPICAL JAK INHIBITOR

NEW for uncontrolled, mild to moderate atopic dermatitis in non-immunocompromised patients aged ≥12 years[1]

- **Clear or almost clear skin** (IGA 0/1)* in >50% of patients at week 8 (53.8% vs 15.1% and 51.3% vs 7.6% vehicle†; $P<0.0001$)[1,2]
- **Meaningful itch relief** (Itch NRS4) in >50% of patients at week 8 (52.2% vs 15.4% and 50.7% vs 16.3% vehicle†; $P<0.0001$)[1,2‡]
  - **Itch NRS4 response seen as early as day 3** (18.4% OPZELURA vs 4.2% vehicle and 13.2% OPZELURA vs 0% vehicle†)[3]

OPZELURA was studied in 1249 adult and adolescent patients ≥12 years of age in 2 identically designed double-blind, randomized, vehicle-controlled trials (TRuE-AD1 and TRuE-AD2). In both studies, patients had an affected BSA of 3%-20% and an IGA score of 2 or 3 on a severity scale of 0-4. Patients were randomized to monotherapy with OPZELURA or vehicle BID for 8 weeks.[1,2]

*With a ≥2-grade improvement from baseline.[1]

†In TRuE-AD1 and TRuE-AD2, respectively.[1,2]

‡≥4-point improvement in NRS among patients with a score of ≥4 at baseline.[1]

BID=twice daily; BSA=body surface area; IGA=Investigator's Global Assessment; JAK=Janus kinase; NRS=numeric rating scale.

Discover the difference at OpzeluraHCP.com

Incyte Dermatology

INDICATION

OPZELURA is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Limitation of Use:

Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death. Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease.**
- **Invasive fungal infections, including candidiasis and pneumocystosis.**
- **Bacterial, viral, and other infections due to opportunistic pathogens.**

Avoid use of OPZELURA in patients with an active, serious infection, including localized infections.

If a serious infection develops, interrupt OPZELURA until the infection is controlled. Carefully consider the benefits and risks of treatment prior to initiating OPZELURA in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with OPZELURA.

No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider evaluating patients for latent and active TB infection prior to administration of OPZELURA. During OPZELURA use, monitor patients for the development of signs and symptoms of TB.

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Please see additional Important Safety Information on following page.

Please see Brief Summary of Full Prescribing Information on following pages.

Opzelura™
(ruxolitinib) cream 1.5%

IMPORTANT SAFETY INFORMATION for OPZELURA™ (ruxolitinib) cream 1.5% (continued)

SERIOUS INFECTIONS (continued)

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B or hepatitis C.

MORTALITY

Higher rate of all-cause mortality, including sudden cardiovascular death, has been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Patients who are current or past smokers are at additional increased risk. Non-melanoma skin cancers, including basal cell and squamous cell carcinoma, have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and following treatment as appropriate.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if these symptoms occur.

THROMBOSIS

Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis has been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated.

Thromboembolic events were observed in clinical trials with OPZELURA. There was no clear relationship between platelet count elevations and thrombotic events. OPZELURA should be used with caution in patients who may be at increased risk of thrombosis.

Thrombocytopenia, Anemia and Neutropenia

Thrombocytopenia, anemia and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations

Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

Adverse Reactions

The most common adverse reactions (≥1%) are nasopharyngitis (3%), diarrhea (1%), bronchitis (1%), ear infection (1%), eosinophil count increased (1%), urticaria (1%), folliculitis (1%), tonsillitis (1%), and rhinorrhea (1%).

Pregnancy

There will be a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 855-4MEDINFO or 855-463-3463.

Lactation

Advise women not to breastfeed during treatment with OPZELURA and for four weeks after the last dose (approximately 5 elimination half-lives).

Please see Brief Summary of Full Prescribing Information on following pages.

References: 1. Opzelura. Prescribing Information. Incyte Corporation; 2021. **2.** Papp K, Szepietowski JC, Kircik L, et al. Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: results from 2 phase 3, randomized, double-blind studies. *J Am Acad Dermatol.* Published online May 3, 2021. doi:10.1016/j.jaad.2021.04.085. **3.** Data on file. Incyte Corporation. 2021.

Opzelura™ (ruxolitinib) cream 1.5%

OPZELURA™ (ruxolitinib) cream, for topical use

Brief Summary of FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE: OPZELURA is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Limitation of Use: Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS

SERIOUS INFECTIONS
Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death *[see Warnings and Precautions and Adverse Reactions]*.

Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease.**
- **Invasive fungal infections, including candidiasis and pneumocystosis.**
- **Bacterial, viral, and other infections due to opportunistic pathogens.**

Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. If a serious infection develops, interrupt OPZELURA until the infection is controlled.

The risks and benefits of treatment with OPZELURA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with OPZELURA *[see Warnings and Precautions]*.

MORTALITY
Higher rate of all-cause mortality, including sudden cardiovascular death have been observed in patients treated with oral Janus kinase inhibitors for inflammatory conditions *[see Warnings and Precautions]*.

MALIGNANCIES
Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions *[see Warnings and Precautions]*.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)
Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions *[see Warnings and Precautions]*.

THROMBOSIS
Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis has been observed at an increased incidence in patients treated with oral Janus kinase inhibitors for inflammatory conditions compared to placebo. Many of these adverse reactions were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS

Serious Infections: Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving oral janus kinase inhibitors. Serious lower respiratory tract infections were reported in the clinical development program with topical ruxolitinib. Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating OPZELURA in patients: with chronic or recurrent infection; with a history of a serious or an opportunistic infection; who have been exposed to tuberculosis; who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or with underlying conditions that may predispose them to infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with OPZELURA. Interrupt OPZELURA if a patient develops a serious infection, an opportunistic infection, or sepsis. Do not resume OPZELURA until the infection is controlled.

Tuberculosis: No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider evaluating patients for latent and active TB infection prior to administration of OPZELURA. During OPZELURA use, monitor patients for the development of signs and symptoms of TB.

Viral Reactivation: Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Hepatitis B and C: The impact of Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA on chronic viral hepatitis reactivation is unknown. Patients with a history of hepatitis B or C infection were excluded from clinical trials.

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B or hepatitis C.

Mortality: A higher rate of all-cause mortality, including sudden cardiovascular death was observed in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA.

Malignancy and Lymphoproliferative Disorders: Malignancies, including lymphomas, were observed in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients with a known malignancy (other than successfully treated non-melanoma skin cancers), patients who develop a malignancy, and patients who are current or past smokers.

Non-melanoma Skin Cancers: Non-melanoma skin cancers including basal cell and squamous cell carcinoma have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and following treatment as appropriate.

Major Adverse Cardiovascular Events (MACE): Major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal stroke were observed in clinical trials of Janus kinase inhibitors used to treat inflammatory conditions. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if these symptoms occur.

Thrombosis: Thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE) and arterial thrombosis, has been observed at an increased incidence in patients treated with oral Janus kinase inhibitors for inflammatory conditions compared to patients treated with placebo. Many of these adverse reactions were serious and some resulted in death. Thromboembolic events were observed in clinical trials with OPZELURA. There was no clear relationship between platelet count elevations and thrombotic events. OPZELURA should be used with caution in patients who may be at increased risk of thrombosis.

Thrombocytopenia, Anemia and Neutropenia: Thrombocytopenia, anemia and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations: Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

ADVERSE REACTIONS

Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In two double-blind, vehicle-controlled clinical trials (Trials 1 and 2), 499 subjects 12 years of age and older with atopic dermatitis were treated with OPZELURA twice daily for 8 weeks. In the OPZELURA group, 62% of subjects were females, and 71% of subjects were White, 23% were Black, and 4% were Asian. The adverse reactions reported by ≥ 1% of OPZELURA-treated subjects and at a greater incidence than in the vehicle arm through week 8 are as follows for OPZELURA (N=499) vs Vehicle (N=250), respectively: Subjects with any treatment emergent adverse event (TEAE) 132 (27%) vs 83 (33%), Nasopharyngitis 13 (3%) vs 2 (1%), Bronchitis 4 (1%) vs 0 (0%), Ear infection 4 (1%) vs 0 (0%), Eosinophil count increased 4 (1%) vs 0 (0%), Urticaria 4 (1%) vs 0 (0%), Diarrhea 3 (1%) vs 1 (<1%), Folliculitis 3 (1%) vs 0 (0%), Tonsillitis 3 (1%) vs 0 (0%), and Rhinorrhea 3 (1%) vs 1 (<1%).

Adverse reactions that occurred in Trials 1 and 2 in < 1% of subjects in the OPZELURA group and none in the vehicle group were: neutropenia, allergic conjunctivitis, pyrexia, seasonal allergy, herpes zoster, otitis externa, Staphylococcal infection, and acneiform dermatitis.

DRUG INTERACTIONS

Drug interaction studies with OPZELURA have not been conducted. Ruxolitinib is known to be a substrate for cytochrome P450 3A4 (CYP3A4). Inhibitors of CYP3A4 may increase ruxolitinib systemic concentrations whereas inducers of CYP3A4 may decrease ruxolitinib systemic concentrations.

Strong Inhibitors of CYP3A4: Avoid concomitant use of OPZELURA with strong inhibitors of CYP3A4 as there is a potential to increase the systemic exposure of ruxolitinib and could increase the risk of OPZELURA adverse reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry: There will be a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 1-855-463-3463.

Risk Summary: Available data from pregnancies reported in clinical trials with OPZELURA are not sufficient to evaluate a drug-associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of ruxolitinib to pregnant rats and rabbits during the period of organogenesis resulted in adverse developmental outcomes at doses associated with maternal toxicity.

The background risks of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies carry some risk of birth defects, loss, or other adverse outcomes. The background risk in the U.S. general population of major birth defects and miscarriage is 2-4% and 15-20%, respectively.

Data

Animal Data: Ruxolitinib was administered orally to pregnant rats or rabbits during the period of organogenesis, at doses of 15, 30 or 60 mg/kg/day in rats and 10, 30 or 60 mg/kg/day in rabbits. There were no treatment-related malformations at any dose. A decrease in fetal weight of approximately 9% was noted in rats at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 22 times the clinical systemic exposure at the maximum recommended human dose (MRHD); the clinical systemic exposure from ruxolitinib cream, 1.5% applied twice daily to 25-40% body surface area is used for calculation of multiples of human exposure. In rabbits, lower fetal weights of approximately 8% and increased late resorptions were noted at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 70% the MRHD clinical systemic exposure. In a pre-and post-natal development study in rats, pregnant animals were dosed with ruxolitinib from implantation through lactation at doses up to 30 mg/kg/day. There were no drug-related adverse effects on embryofetal survival, postnatal growth, development parameters or offspring reproductive function at the highest dose evaluated (3.1 times the MRHD clinical systemic exposure).

Lactation

Risk Summary: There are no data on the presence of ruxolitinib in human milk, the effects on the breastfed child, or the effects on milk production. Ruxolitinib was present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the serious adverse findings in adults, including risks of serious infections, thrombocytopenia, anemia, and neutropenia, advise women not to breastfeed during treatment with OPZELURA and for approximately four weeks after the last dose (approximately 5 elimination half-lives).

Data: Lactating rats were administered a single dose of [14C]-labeled ruxolitinib (30 mg/kg) on postnatal Day 10, after which plasma and milk samples were collected for up to 24 hours. The AUC for total radioactivity in milk was approximately 13 times the maternal plasma AUC. Additional analysis showed the presence of ruxolitinib and several of its metabolites in milk, all at levels higher than those in maternal plasma.

Pediatric Use: The safety and effectiveness of OPZELURA for the topical treatment of atopic dermatitis have been established in pediatric patients aged 12 to 17 years of age with mild-to-moderate atopic dermatitis. Use of OPZELURA in this age group is supported by evidence from Trials 1 and 2 which included 92 subjects aged 12 to 17 years. No clinically meaningful differences in safety or effectiveness were observed between adult and pediatric subjects. The safety and effectiveness of OPZELURA in pediatric patients younger than 12 years of age have not been established.

Juvenile Animal Toxicity Data: Oral administration of ruxolitinib to juvenile rats resulted in effects on growth and bone measures. When administered starting at postnatal day 7 (the equivalent of a human newborn) at doses of 1.5 to 75 mg/kg/day, evidence of fractures occurred at doses ≥ 30 mg/kg/day, and effects on body weight and other bone measures [e.g., bone mineral content, peripheral quantitative computed tomography, and x-ray analysis] occurred at doses ≥ 5 mg/kg/day. When administered starting at postnatal day 21 (the equivalent of a human 2-3 years of age) at doses of 5 to 60 mg/kg/day, effects on body weight and bone occurred at doses ≥ 15 mg/kg/day, which were considered adverse at 60 mg/kg/day. Males were more severely affected than females in all age groups, and effects were generally more severe when administration was initiated earlier in the postnatal period. These findings were observed at systemic exposures that are at least 40% the MRHD clinical systemic exposure.

Geriatric Use: Of the 1249 total subjects with atopic dermatitis in clinical trials with OPZELURA, 115 were 65 years of age and older. No clinically meaningful differences in safety or effectiveness were observed between patients less than 65 years and patients 65 years and older.

PATIENT COUNSELING INFORMATION

Advise the patient or caregivers to read the FDA-approved patient labeling (Medication Guide).

Infections: Inform patients that they may be at increased risk for developing infections, including serious infections, when taking Janus kinase inhibitors. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of an infection. Advise patients that Janus kinase inhibitors increase the risk of herpes zoster, and some cases can be serious.

Malignancies and Lymphoproliferative Disorders: Inform patients that Janus kinase inhibitors may increase the risk for developing lymphomas and other malignancies including skin cancer. Instruct patients to inform their health care provider if they have ever had any type of cancer. Inform patients that periodic skin examinations should be performed while using OPZELURA.

Major Adverse Cardiovascular Events: Advise patients that events of major adverse cardiovascular events (MACE) including non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death, have been reported in clinical studies with Janus kinase inhibitors used to treat inflammatory conditions. Instruct all patients, especially current or past smokers or patients with other cardiovascular risk factors, to be alert for the development of signs and symptoms of cardiovascular events.

Thrombosis: Advise patients that events of DVT and PE have been reported in clinical studies with Janus kinase inhibitors used to treat inflammatory conditions. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of a DVT or PE.

Thrombocytopenia, Anemia and Neutropenia: Advise patients of the risk of thrombocytopenia, anemia, and neutropenia with OPZELURA. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of thrombocytopenia, anemia or neutropenia *[see Warnings and Precautions]*.

Administration Instructions: Advise patients or caregivers that OPZELURA is for topical use only *[see Dosage and Administration]*.

Advise patients to limit treatment to 60 grams per week.

Pregnancy: Inform patients to report their pregnancy to Incyte Corporation at 1-855-463-3463 *[see Use in Specific Populations]*.

Lactation: Advise a patient not to breastfeed during treatment with OPZELURA and for four weeks after the last dose *[see Use in Specific Populations]*.

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Atopic dermatitis

BY ZELMA C. CHIESA FUXENCH, MD, MSCE

If there ever were a more exciting time to be involved in the field of atopic dermatitis (AD), it's now. The articles herein seek to further advance our global understanding of AD with a focus on topics as diverse as treatment satisfaction from the patient's perspective, examination of health inequities in the care of patients with AD, and reconsideration of established opinions about basic skin care practices, such as bathing.

Dr. Fuxench

It is no secret that the management of AD can be quite complex and there are many intricacies to consider when taking care of patients with this disease. While many of us may be patting ourselves in the back for thinking we are doing an excellent job in managing our patients with AD, a study by Cheng et al. (page 8) that examined treatment satisfaction in adults with AD found that this may not be the case and that greater effort is needed to better understand predictors of patient satisfaction among patients with AD and how this relates to patterns of health care use. Their findings support that low income, no insurance coverage, and increased comorbidities, among other factors, are related to worse satisfaction scores.

Advances in our understanding of disease pathogenesis in AD has led to an increased understanding of this disease with development of newer therapeutic approaches that hold great promise for patients whose disease remains poorly controlled despite the advent of biologic therapies such as dupilumab. Janus kinase (JAK) inhibitors are one group of such agents. Findings from the JADE COMPARE study provide further evidence that not only do JAK inhibitors, such as abrocitinib, improve signs of skin inflammation in AD but they are particularly useful for managing itch, the hallmark symptom of AD, quickly and effectively (page 10).

However, while much progress has been made in our understanding of the immunological basis of AD, there is still much work to be done with respect to understanding differences in disease risk and persistence among groups. Findings from the study by Chovatiya et al. (page 12) remind us of health inequities that exist among patients with AD, including higher out-of-pocket costs and increase in the use of step-therapy with systemic therapies. If we are to improve health care disparities in AD, strategies for tackling these differences are much needed not only at a patient level but at a societal level as well.

Finally, the last article (page 14) speaks to the age-old question in AD, to bathe more or not to bathe? Noreen Heer Nicol, PhD, RN, FNP, discusses the frustrations surrounding this topic among patients, caregivers, and health care providers and stresses the need for good quality studies in this area. She also discusses the rationale behind the 3-minute rule for bathing and application of moisturizers from the National Eczema Association, as well as a stepwise management model for a basic skin care regimen in AD and recommendations from the Atopic Dermatitis Yardstick. In a world where treatment options for AD are becoming more available, findings from this work remind us of the importance of a basic skin care regimen that is easy to implement and can help us better manage AD.

Dr. Chiesa Fuxench is assistant professor of dermatology at the University of Pennsylvania, Philadelphia. Her clinical practice is focused on the care of patients with inflammatory skin diseases, including AD. Her research is focused on improving the understanding of the epidemiology, natural course, and comorbidities of these diseases through investigator-driven collaborative work and by engaging in clinical trials for novel therapeutic interventions. She has received research grants from Lilly, LEO Pharma, Menlo Therapeutics, Regeneron, Sanofi, Tioga, and Vanda for work related to AD; has served as a consultant for the Asthma and Allergy Foundation of America, National Eczema Association, AbbVie, Incyte Corporation, and Pfizer; and has received honoraria for CME work in AD sponsored by education grants from Regeneron/Sanofi.

Dermatology News

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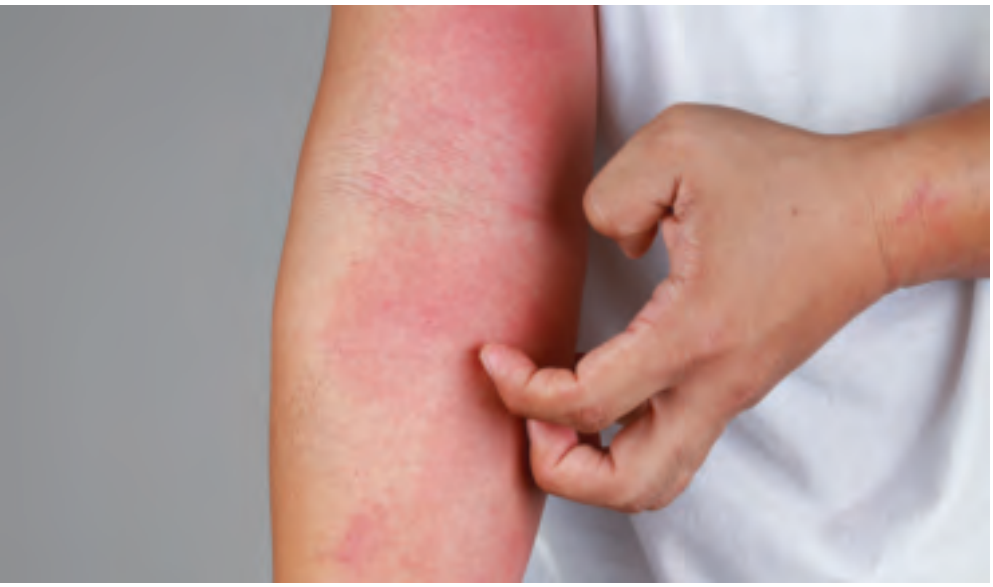
What factors influence treatment satisfaction among adults with atopic dermatitis?

BY DOUG BRUNK

Atopic dermatitis (AD) is associated with lower patient satisfaction scores in adults, suggesting there are unmet needs in clinical AD management.

Satisfaction scores were higher when specialists prescribed systemic therapy, but were lower when nonspecialists prescribed systemic therapy and when specialists prescribed only topical therapy.

Those are among key findings from an analysis of the Medical Expenditure Panel Surveys reported by Brian T. Cheng at the Revolutionizing Atopic Dermatitis symposium.



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"AD management is complex," said Mr. Cheng, a medical student at Northwestern University, Chicago. "It includes patient education about trigger avoidance, over-the-counter and prescription topical therapies, as well as systemic therapies. Previous studies have shown major decrements to quality of life as well as atopic and non-atopic comorbidities in these patients. The burden of AD and their comorbidities, as well as their management, may impact patient satisfaction."

Prior studies have demonstrated that patient satisfaction is associated with improvements in clinical outcomes, increased patient retention, and reduced malpractice claims (Br J Dermatol. 2001 Oct;145[4]:617-23, Arch Dermatol 2008 Feb;144[2]:263-5). However, since data on patient satisfaction in AD are limited, Mr. Cheng and the study's senior author, Jonathan I. Silverberg, MD, PhD, MPH, set out to examine overall patient satisfaction among adults with AD, to determine associations of patient satisfaction with patterns of health care utilization, and to identify predictors of higher satisfaction among these adults.

The researchers conducted a cross-sectional retrospective analysis of 3,810 patients from the 2000-2015 Medical Expenditure Panel Surveys, representative surveys of the U.S. noninstitutionalized population conducted annually by the Agency for Healthcare Research and Quality. They used ICD-9 codes 691 and 692 to determine AD diagnosis and five Consumer Assessment of Health Plans Survey (CAHPS) questions to assess patients' satisfaction with their clinicians. "These questions have been extensively validated to correlate with global satisfaction," Mr. Cheng said. "These are not disease-specific and allow for comparison across multiple diseases."

Next, the researchers created a composite satisfaction score based on the methods of Anthony Jerant, MD, of the University of California, Davis, and colleagues (J Gen Intern Med. 2019 Aug;34[8]:1459-66). They adjusted each question in the CAHPS survey to have an equal weight and then summed these into a composite satisfaction score. "We examined patient satisfaction comparing across diseases, and based on the guidelines from the AHRQ to isolate that impact of patient-physician interaction, we adjusted for sociodemographics, mental and physical health status, self-reported health rating, as well as multimorbidity and comorbid diseases."

Compared with adults who are healthy, adults with AD had lower patient satisfaction overall. "Moreover, people with AD had lower satisfaction compared to those with psoriasis, which may reflect more substantial itch burden as well as the greater comorbid disease challenges in management," Mr. Cheng said. "It may also reflect the renaissance in psoriasis treatment over the last 10-20 years, giving a wider spectrum of treatment and thus a higher patient satisfaction."

Among adults with AD, lower satisfaction was consistent across all domains of CAHPS. For the question of "How often health providers listen carefully to you," the adjusted OR (aOR) was 0.87 ($P = .008$). For the question of "How often health providers explain things in a way that was easy to understand," the aOR was 0.89 ($P = .003$). For the question of "How often health providers spent enough time with

you," the aOR was 0.86 ($P = .0001$). For "How often providers showed respect for what you had to say," the aOR was 0.91 ($P = .02$).

Recognizing that treatment regimens are complex and used differently by provider type, the researchers examined interactions between specialists (dermatologists and allergists) and treatment type. "Previous studies found dermatologists treat more severe, chronic AD," Mr. Cheng said. "We found here that there was lower satisfaction among those treated with topical therapy and by specialists, which may reflect inadequate disease control. We also found lower satisfaction among those treated with systemic therapy by primary care physicians. This may reflect that these patients are not achieving optimal therapy. We found that satisfaction was highest among those treated with systemic therapy and by dermatologists and allergists."

Socioeconomic, racial/ethnic, and health care disparities were observed in terms of satisfaction among this cohort. The following characteristics were significantly associated with lower patient satisfaction, compared with the general cohort of adults with AD: poor to low income (aOR, –1.82; P less than .0001), multiracial/other race (aOR, –2.34; $P = .0001$), Hispanic ethnicity (aOR, –1.40; $P = .007$), and having no insurance coverage (aOR, –4.53; P less than .0001).

> **"There's a need here for multidisciplinary care** to ensure that all of these comorbidities and the full spectrum of symptoms are being managed adequately."

"Moreover, those with multimorbidity had even lower satisfaction," Mr. Cheng said. "In previous studies, AD has been linked with many other comorbidities. This may reflect that these patients are not being adequately managed overall. So, there's a need here for multidisciplinary care to ensure that all of these comorbidities and the full spectrum of symptoms are being managed adequately."

He concluded that future research is needed to determine strategies to optimize patient satisfaction in adults with AD.

"I'm not sure how much more provocative you can get in terms of data," added Dr. Silverberg, director of clinical research and contact dermatitis at George Washington University, Washington. "It's really eye-opening. I think many clinicians may feel like they're doing a perfect job in managing this disease. These data suggest that at least at the national level that may not be the case."

Mr. Cheng reported having no financial disclosures. Dr. Silverberg reported that he is a consultant to and/or an advisory board member for several pharmaceutical companies. He is also a speaker for Regeneron and Sanofi and has received a grant from Galderma.

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Commentary by Dr. Chiesa Fuxench:

HOW GOOD IS GOOD ENOUGH in terms of atopic dermatitis (AD) disease control? As physicians, is it sufficient to just focus on controlling disease signs and symptoms at first, as one would naturally assume that this in turn would lead to improvements in quality of life and decreased disease burden? What is the end goal for AD, if there even is one? How do we begin to engage more with patients and caretakers in the process of shared decision-making when it comes to treatment decisions and patient satisfaction?

Perhaps a first step is to humbly recognize that our understanding of what we think is the best treatment option for our patients and/or whether or not the treatment is considered successful in terms of disease control may not always align with the patients' or caregivers' perception and/or experience. There is increasing evidence in the literature to support that AD can be a lifelong disease for many patients and, for many of us who care for these patients, it is no secret that patient satisfaction with treatment can oftentimes be low.

We should welcome the findings from Chen and colleagues, which further our understanding of treatment satisfaction in adult patients with AD, including examining predictors of patient satisfaction. Not surprisingly, patients with AD were found to have lower satisfaction overall when compared not only with healthy controls but with patients with psoriasis as well. The authors hypothesized that this could be caused by patients with AD having a higher burden of disease with respect to symptoms (such as higher itch burden), lack of treatment options, and the complexities of managing a chronic disease that can be associated with other longstanding comorbidities. Interestingly, the study investigators found that patients treated with systemic therapy in the primary care setting and those treated with topical treatments by dermatologists presented with lower satisfaction scores, whereas those treated with systemic agents by dermatologists tended to have higher satisfaction scores. The authors suggest that this in part could be explained by poor disease control in either setting.

I recently stumbled upon a quote attributed to William Osler, which states, "It is much more important to know what sort of a patient has a disease than what sort of a disease the patient has." In other words, who is this person in front of me? What are their views and beliefs, and what do they value as important? If we are to further improve the care and quality of life in patients with AD – or any disease for that matter – we must continue to strive to understand how patients perceive their disease, and the control of their disease, as well as what factors are driving those beliefs.

Itch response faster with JAK inhibitor, when compared with dupilumab, in phase 3 study

BY LAIRD HARRISON

An experimental oral Janus kinase 1 (JAK1) inhibitor, abrocitinib, showed greater itch reduction after 2 weeks of treatment than dupilumab in patients with moderate to severe atopic dermatitis (AD), in a multicenter, randomized trial.

In addition, in the study, those on 200-mg and 100-mg daily doses of abrocitinib experienced significantly greater reductions in signs and symptoms of AD at 12 and 16 weeks, than those on placebo, the authors reported. The findings from the JADE COMPARE trial, published in the New England Journal of Medicine (2021 Mar 25;384[12]:1101-12), suggest abrocitinib will provide clinicians with another treatment option for patients who don't get adequate relief from either topical medications or dupilumab. Abrocitinib is associated with a different set of adverse reactions than dupilumab, according to investigators.

In 2017, dupilumab (Dupixent) became the first systemic drug approved by the Food and Drug Administration specifically for AD, though systemic steroids and other immunosuppressant drugs are sometimes prescribed. A monoclonal antibody delivered by subcutaneous injection, dupilumab binds to interleukin-4 receptors to block signaling pathways involved in AD; it is now approved for treatment of patients with moderate to severe AD down to age 6 years.

"It is sort of the bar for efficacy and for safety in those patients, because that's what we have right now," said one of the JADE COMPARE investigators and study author, Jonathan I. Silverberg, MD, PhD, MPH, associate professor of dermatology and director of clinical research and contact dermatitis at George Washington University, Washington, said in an interview. "For any new therapy coming to market, we really do want to understand how it compares to what's out there."

Abrocitinib is a small molecule that inhibits JAK1, which is thought to modulate multiple cytokines involved in AD, including interleukin (IL)–4, IL-13, IL-31, IL-22, and thymic stromal lymphopoietin. Two other JAK1 inhibitors, baricitinib and upadacitinib, are also being investigated as systemic treatments for AD.

In JADE COMPARE, people with moderate to severe AD from 18 countries entered a 28-day screening period during which they discontinued treatments. They began using emollients twice a day at least 7 days before being randomly assigned to a treatment group, and continued on topical medication once daily. Topical treatments included low- or medium-potency topical glucocorticoids, calcineurin inhibitors, and phosphodiesterase-4 inhibitors.

The researchers randomly assigned 838 to trial groups: 226 received 200 mg of abrocitinib orally once a day, 238 received 100 mg of abrocitinib once a day, 243 received a 300-mg dupilumab injection every other week, and 131 received placebo versions of both medications, for 16 weeks. The mean age of the patients overall was about 38 years; about two-thirds were White.

At 2 weeks, almost half (49.1%) of the patients on 200 mg of abrocitinib and 31.8% of those on the 100-mg dose had an itch response, defined as at least a 4-point improvement from baseline in the 0-10 Peak Pruritus Numerical Rating Scale. This was compared with 26.4% of those on dupilumab and 13.8% of those on placebo.

And at 12 weeks, more of the patients in the 200-mg abrocitinib group than in the other groups had an Investigator's Global Assessment (IGA) response (defined as clear or almost clear) and more had an Eczema Area and Severity Index (EASI-75) response (defined as an improvement of at least 75%). (See Table.) EASI-75 and IGA responses at week 12 were the primary outcomes of the study.

> "For any new therapy coming to market, we really do want to understand **how it compares to what's out there**."

The differences between both abrocitinib groups and the placebo group were statistically significant by all these measures ($P < .001$). The difference between the 200-mg abrocitinib and the dupilumab group was only significant for itch at 2 weeks, and the difference in itch response between the 100-mg group and the dupilumab group at 2 weeks was not significant ($P < .2$).

At 16 weeks, the EASI-75 response (a secondary endpoint) among those on either dose of abrocitinib was not significantly different than among those on dupilumab (71% and 60.3% among those on 200 mg and 100 mg, respectively; and 65.5% among those on dupilumab, compared with 30.6% of those on placebo).

The study didn't have sufficient statistical power to fully explore the comparison to dupilumab, and future trials will go deeper into the comparison, said one of the study authors, Melinda Gooderham, MsC,

MD, an assistant professor at Queen's University, Kingston, Ont. Still, in this trial, abrocitinib demonstrated a clear advantage in the speed and depth of efficacy, Dr. Silverberg noted. "The 100-mg dose of abrocitinib was about as effective as, or maybe slightly less effective than, dupilumab, and the 200-mg dose was more effective than dupilumab." The overall incidence of adverse events was higher in the 200-mg abrocitinib arm than in the other groups, but the incidence of serious or severe adverse events, and the incidence of adverse events that resulted in discontinuing the medication, were similar across the trial groups.

However, nausea affected 11.1% of the patients in the 200-mg abrocitinib group and 4.2% of those in the 100-mg abrocitinib group. Acne was also reported in these groups (6.6% and 2.9%, among those on 200 mg and 100 mg, respectively, compared with 1.2% of those on dupilumab and none of those on placebo). In a few of those on abrocitinib, herpes zoster flared up. And median platelet counts decreased among the patients taking abrocitinib, although none dropped below 75,000/mm^3. Serious infections were reported in two patients on abrocitinib, but resolved.

By contrast, only 2.9% of the patients on dupilumab had nausea. But 6.2% in the dupilumab group had conjunctivitis, compared with 1.3% of patients in the 200-mg abrocitinib group and 0.8 in the 100-mg abrocitinib group.

As an oral medication, abrocitinib will appeal to patients who want to avoid injections, and dosing will be easier to adjust, Dr. Silverberg said. On the other hand, he added, dupilumab will have an advantage for patients who don't want to take a daily medication, or who are concerned about the adverse events associated with abrocitinib, particularly those with blood-clotting disorders.

The study was funded by Pfizer. Dr. Silverberg's disclosures included serving as a consultant to companies including AbbVie, Pfizer, and Regeneron. Several authors are Pfizer employees; other authors had disclosures related to Pfizer and other pharmaceutical companies.

Treatment groups and endpoints

	2-week itch response, %	12-week IGA response, %	12-week EASI-75 response, %
Abrocitinib, 200 mg (n = 226)	49.1	48.4	70.3
Abrocitinib, 100 mg (n = 238)	31.8	36.6	58.7
Dupilumab (n = 243)	26.4	36.5	58.1
Placebo (n = 131)	13.8	14.0	27.1

MDedge News

Note: All patients had moderate-to-severe AD and were receiving background topical therapy.

Source: N Engl J Med. 2021;384:1101-12

Commentary by Dr. Chiesa Fuxench:

ITCH, THE HALLMARK symptom of atopic dermatitis, contributes highly to the burden of AD and often results in detriments in sleep and health-related quality of life. As such, quick control of itch is critical when caring for patients with this disease.

There is absolutely no question that approval of the first biologic for AD, dupilumab, has been a game changer for many patients. Oral Janus kinase 1 inhibitors, such as abrocitinib, offer another sign of hope for our patients with AD. Results from multiple studies not only of abrocitinib but with other JAK inhibitors such as upadacitinib and baricitinib are promising. Yet concern with respect to their safety profile has resulted in the approval of these medications being further delayed. When dupilumab is considered an overall efficacious and safe treatment option for AD, where does the need for JAK inhibitors lie? For starters, it is not surprising that not all patients with AD will improve on dupilumab and others may only show partial response. For others, it may be an issue of tolerability (such as intolerance to injections) and/or comorbidities (such as a history of eye disorders). Because itch is associated with high burden in AD, quick control of symptoms is critical. Direct comparisons of the effectiveness and safety of dupilumab and JAK inhibitors are limited by the small number of studies completed thus far. Nevertheless, the results of the JADE COMPARE study comparing the effectiveness and safety of dupilumab, abrocitinib 100 mg, and abrocitinib 200 mg, summarized in this article, found that patients in the abrocitinib groups achieved greater improvements in itch, compared with dupilumab or placebo at 2 weeks.

While findings from this study support the idea that abrocitinib may result in faster improvements in itch, compared with dupilumab, it is important to note that findings from a prior analysis of randomized phase 3 studies of dupilumab (SOLO 1, SOLO 2, AD ADOL, and CHRONOS) demonstrated this medication can also result in improvements in itch as early as day 2 of treatment when compared with placebo (J Am Acad Dermatol. 2020 Jun;82[6]:1328-36). Still, comparison between studies is often difficult, partly because of differences in study protocols and methods.

The safety of JAK inhibitors is also a topic of investigation. While commonly reported side effects of dupilumab include injection-site reactions, nasopharyngitis, and conjunctivitis, JAK inhibitors are more commonly associated with headache, nausea, nasopharyngitis, upper respiratory tract infection, and lab abnormalities such as decreased platelet counts and lipid elevations. While further work is still needed in this area, potentially long-term, real-world, observational studies, JAK inhibitors appear to be a safe and efficacious alternative for those who are not candidates for dupilumab and would be a much-welcomed tool in our armamentarium of treatments for patients with AD.

Survey spotlights the out-of-pocket burden on Blacks with atopic dermatitis

BY DOUG BRUNK
FROM REVOLUTIONIZING AD 2021

Compared with their non-Black counterparts, Black patients with atopic dermatitis (AD) are significantly more likely to be younger, have lower household incomes, live in an urban setting, and use Medicaid or state assistance. They also have significantly poorer disease control and an increased rate of comorbid skin infections.

Those are among the key findings from a 25-question survey administered to members of the National Eczema Association.

"Black individuals with AD have a unique sociodemographic and disease profile," lead study investigator Raj Chovatiya, MD, PhD, said during the Revolutionizing Atopic Dermatitis symposium. "Out-of-pocket expenses are just one component of the real-world burden faced by this population."

According to Dr. Chovatiya, of the department of dermatology at Northwestern University, Chicago, the clinical phenotype and burden of AD can vary across racial and ethnic groups. Black race, for example, is associated with a higher prevalence of AD, a higher burden of moderate to severe disease, increased rates of allergic comorbidities, greater AD-related impact on health-related quality of life, and more treatment-resistant AD.

"These features can make long-term AD control very difficult," he said. "Given the variable long-term efficacy and safety of current treatments, health care providers and patients often have to combine therapies, seek new treatments, and consider adjunctive approaches – all of which can contribute to increased costs."

AD is also associated with a considerable financial burden, he continued, including direct health care costs, lost work productivity, and out-of-pocket health care expenses. "Previous population-based studies suggest that there are multifactorial increases in overall out-of-pocket health expenses in AD," Dr. Chovatiya said. "Black race in particular is thought to be associated with increased health care utilization in AD, but little is known about the out-of-pocket health care expenses."

To characterize the categories and impact of out-of-pocket health care expenses associated with AD management among Black individuals, he and his colleagues administered a 25-question voluntary survey to 113,502 members of the NEA between Nov. 14 and Dec. 21, 2019. They included adults with a self-reported diagnosis of AD or

> "Our findings ... provide **another piece of evidence for increased financial burden** among Black individuals with AD and support the need for targeted strategies to address these inequities."

children, teens, or young adults who had a caregiver responding for them. In all, 1,118 respondents met inclusion criteria. Questions included those about out-of-pocket expenses for AD over the past 30 days and over the past year, as well as the disease impact on household finances.

The cohort included 75% of individuals with AD; 25% were primary caregivers of children, teens, and young adults with AD.


Dr. Chovatiya

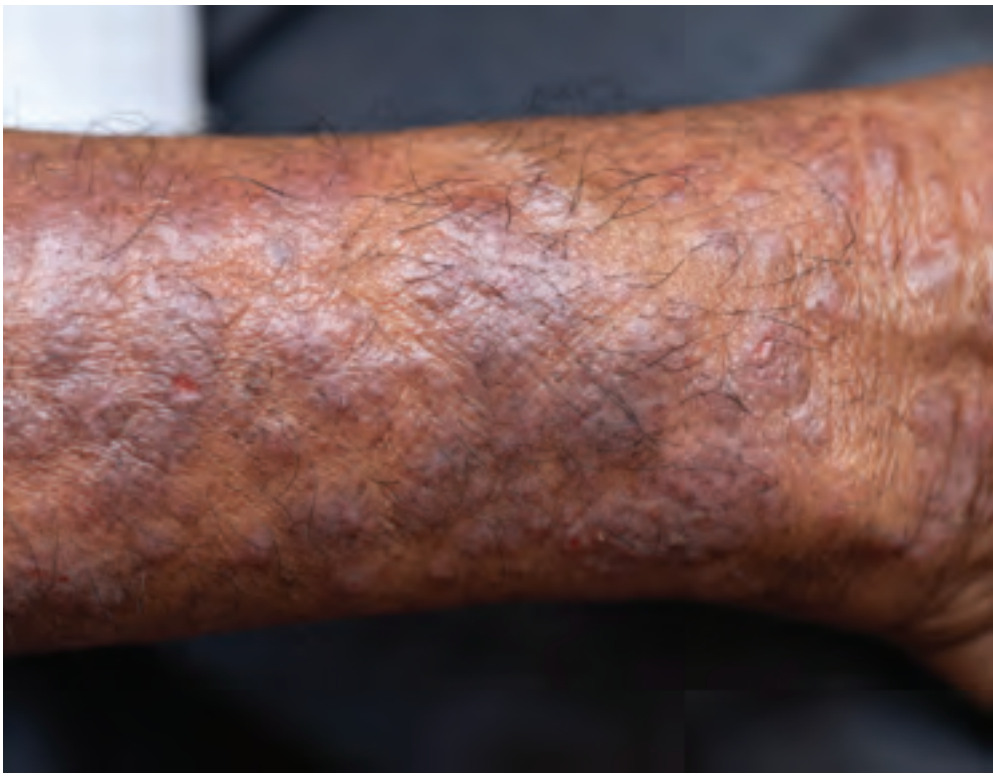
More than three-quarters of respondents (77%) were female; 73% were White, 11% were Black, 6% were Asian, and the remainder were from other ethnic backgrounds. More than half of respondents (58%) had employer-sponsored insurance coverage, and the median annual household income was between $50,000 and $75,000.

Nearly three-quarters of respondents (74%) classified their AD severity as moderate or severe, and 63% reported minimally controlled or somewhat-controlled AD. Black respondents were significantly more likely to be younger, have lower household incomes, live in an urban setting, use Medicaid or state assistance, have poor disease control, and frequent skin infections ($P \leq .02$). "A numerically higher proportion of Black respondents also had increased AD severity and reported the use of step-up therapy with systemic agents, prescription polypharmacy with three or more prescriptions, and a higher monthly out-of-pocket cost," Dr. Chovatiya said.

Compared with their non-Black counterparts, Black survey respondents reported more out-of-pocket costs for prescription medications covered by insurance (74.2% vs. 63.6%; $P = .04$), prescription medications not covered by insurance (65.1% vs. 46.5%; $P = .0004$), ED visits (22.1% vs. 11.8%; $P = .005$), and outpatient laboratory testing (33.3% vs. 21.8%; $P = .01$). Black race was associated with increased

household financial impact from out-of-pocket expenses ($P = .0009$), and predictors of financial impact included minimally controlled AD (adjusted odds ratio, 13.88; $P = .02$), comorbid anxiety and/or depression (aOR, 4.34; $P = .01$), systemic therapy (aOR, 4.34; $P = .003$), out-of-pocket costs that exceeded $200 per month (aOR, 14.28; $P = .0003$), and Medicaid insurance (aOR, 4.02; $P = .03$). Blacks with Medicaid had higher odds of harmful financial impact (aOR, 3.32; $P = .0002$) than respondents who were Black (aOR, 1.81; $P = .04$) or those with Medicaid alone (aOR, 1.39; $P = .04$).

"I looked at some of the findings from recent studies that have talked about this burden, including an increased prevalence among Black children, a higher likelihood of moderate to severe disease, higher rates of ED visits and hospitalizations, and increased prescription medications," Dr. Chovatiya said. "Our findings reflect these racial and socioeconomic disparities and provide another piece of evidence for increased financial burden among Black individuals with AD and support the need for targeted strategies to address these inequities."



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The study received funding support from the NEA. Dr. Chovatiya disclosed that he is a consultant to, a speaker for, and/or a member of the advisory board for AbbVie, Incyte, and Regeneron/Sanofi-Genzyme.

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Commentary by Dr. Chiesa Fuxench:

LIKE MANY AREAS in medicine, health disparities, or the preventable differences in burden of disease experienced by socially disadvantaged groups (such as Blacks, Latinx, Asians, or other minorities), is an expanding area of study in atopic dermatitis. Studies examining differences in disease prevalence, persistence, and overall disease burden in AD across racial groups have previously found that Blacks, compared with Whites, typically present with more severe and persistent disease, as well as increased health care utilization. The relationship among race, social determinants of health, and disease outcomes is complex. It is important to recognize that the concept of race is a social construct and not a biological construct, and by no means should this concept be used to establish one group as inferior to another. Furthermore, while genetic ancestry could potentially account for differences in prevalence and disease persistence in AD, it is most likely that the driving force behind these health inequities in AD are social determinants of health, such as level of education, income disparity, and access to health services among others – which in turn, can lead to poorer control of disease or what appears to be more treatment-resistant AD.

In this survey from the National Eczema Association, researchers found that Black respondents were more likely to be younger, have lower household incomes, use Medicaid or state assistance, and also have overall poor disease control. The researchers also found that Black patients reported an increase in the use of step-up therapy with systemic agents, polypharmacy with prescriptions of three or more agents, which could be interpreted to mean poorer disease control, and increased monthly out-of-pocket costs. If this does not raise concern for the influence of systemic racism in the care of patients with AD, I don't know what would. More work is desperately needed in this area, not only in dermatology, but in medicine overall.

Lastly, the authors conclude that their findings further reflect the disparities seen among groups in AD and that targeted strategies to address these inequalities are needed. But what exactly are those targeted approaches? Perhaps we should begin by making a true effort to recognize that not all patients with AD start on the same level playing field. Whereas economic stability, increased level of education with presumed increased health literacy, and adequate access to health care services are a given for some, not all patients share this advantage, and we must be cognizant of these differences when first embarking on the process of treatment discussion and treatment selection with our patients.

Bathing now more widely accepted as a treatment strategy for patients with eczema

BY DOUG BRUNK
FROM REVOLUTIONIZING AD 2020

According to Noreen Heer Nicol, PhD, RN, FNP, frustration still exists for patients, families, and health care providers regarding the lack of consensus that routine bathing is good for patients with atopic dermatitis.

During the Revolutionizing Atopic Dermatitis symposium, she said that conflicting and vague guidelines currently exist on the topic.


Dr. Nicol

"This stems from the fact that we just don't have good studies," said Dr. Nicol, associate dean and associate professor of nursing at the University of Colorado at Denver, Aurora. "Particularly, we don't have randomized, controlled trials on the effects of water and bathing. It's not just parents that are frustrated, but health care providers are as well."

In an observational analysis, researchers evaluated results from three online surveys of dermatologists, allergists, and immunologists, and primary care physicians regarding routine bathing frequency recommendations for children with AD (Pediatr Dermatol. 2015;32[4]:e194-6). It found that PCPs recommended daily bathing less than 50% of the time, while specialists recommended daily bathing more than 50% of the time.

"It seems like the PCPs have embraced that old dermatology notion when bathing was avoided in patients with AD," Dr. Nicol said. "This lack of consensus on the basic daily care steps in AD management causes a great deal of confusion amongst patients, families, and young health care providers, in particular," she added.

She believes that this goes back to a century-long debate about the pros and cons of bathing in AD. "We used to say that bathing will dry the skin out if you take a bath or a shower without immediately applying something like a good moisturizer. That's where the 3-minute rule came along from the National Eczema Association, meaning that bathing hydrates the stratum corneum if you take a bath or a shower and you immediately apply that good moisturizer within 3 minutes to retain that hydration and keep the barrier intact and flexible."

Dr. Nicol presented a stepwise management model that she has published many times over the years (see Pediatr Nursing. 2020;46[2]:92-8 and J Allergy Clin Immunol Pract. 2019;7[1]:1-16).

Step 1 consists of basic care, including skin hydration/bathing, application of a daily moisturizer, avoiding irritants, and identifying and addressing specific triggers. "This is the foundation for every step as you go forward," she explained. Soak-and-seal has been a mainstay of treatment at National Jewish Health, she noted. "By that, I mean taking a soaking 10-15 minute bath in warm water daily. Gently pat away excess water. Immediately apply skin medications or moisturizer within 3 minutes. Using a gentle fragrance-free, dye-free cleanser to clean skin is also important. Avoid scrubbing."

A review article on bathing and associated treatments in AD was published in 2017 and includes 144 references to bathing studies (Am J Clin Dermatol. 2017;18[1]:45-57). A separate recommendation known as the "AD Yardstick" elaborated on the definition of basic skin care for nonlesional AD (Ann Allergy Asthma Immunol. 2018 Jan;120[1]:10-22.e2). Besides recommending the liberal and frequent application of moisturizers, it suggests management with warm baths or showers using nonsoap cleansers, usually once per day, followed by application of a moisturizer, even on clear areas.

"This is now what people are thinking as the basis of skin care in patients with AD," Dr. Nicol said. "Warm baths and showers don't look so controversial anymore. This model nicely lays out what we want people to remember. In the past, many times we just skipped that important step of telling people about bathing."

In a small 2009 study, researchers conducted a quantitative assessment of combination bathing and moisturizing regimens on skin hydration in AD (Pediatr Dermatol. May-Jun 2009;26[3]:273-8). They found that

> "Bathing hydrates the stratum corneum if you take a bath or a shower and you immediately apply that good moisturizer within 3 minutes **to retain that hydration and keep the barrier intact**."

bathing followed by application of a moisturizer provides modest hydration benefits, though less than that of simply applying moisturizer alone. "That has not been the case for most of us who are bathing advocates," Dr. Nicol said. "We believe that there is an additional hydration

that's gained from bathing and moisturizers done properly."

In an earlier retrospective study of 28 patients referred to a tertiary care center for refractory chronic pruritic eruptions, researchers found that a plain-water 20-minute soak followed by smearing of midstrength corticosteroid ointment led to clearing or dramatic improvement of the lesions (Arch Dermatol. 2005;14:1556-9). The authors recommended prospective studies to confirm the findings. In a separate review of medical literature, researchers explored the role of frequent bathing in the treatment of pediatric AD (Ann Allergy Asthma Immunol. 2016;117[1]:9-13). They found that the weight of evidence suggests that the frequent soak-and-smear bathing is preferred to infrequent bathing in the management of AD. Frequent bathing was defined as bathing at least once a day, while infrequent bathing was defined as bathing less than once a day.

"Bleach baths have received much attention in recent years, and have been endorsed by multiple AD guidelines, though not to the same degree as regular bathing," Dr. Nicol said. "Right now, you can find almost as much literature for this practice as against it. The populations that seem to value beach baths the most, however, are those with frequent infections, particularly those who are methicillin resistant. Most people recommend a maximum of two to three times per week but only with an active infection. Care must be taken to avoid additional drying or irritation of the skin from bleach." Many bleach bath recipes call for adding one-eighth to one-half of a cup of bleach to a tub full of water.

Cavan Images/Getty Images

Dr. Nicol disclosed that she has served as an advisory board member for Eli Lilly.

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Commentary by Dr. Chiesa Fuxench:

TO BATHE OR NOT TO BATHE, why is this still even a question? Countless times during my clinics caring for patients with atopic dermatitis (AD), I hear the same statements repeated over and over: "Bathing is bad, and I was told I should not do this often," "I was told bathing dries my skin out and so I only do this a few times per week," or "I don't know what is right, bathing less or more, as I have been told differently by different doctors." Trust me, I share your frustration. Past dogma in AD has been that patients should bathe less as bathing dries out the skin more, which can then lead to worsening of this disease. Interestingly, for such a well-established dogma, there seems to be little evidence to support it. On the contrary, recent literature supports the idea that bathing or showering, followed by application of moisturizers, is beneficial for patients with AD as it leads, among other things, to increased hydration of the skin. Speaking of moisturizers, there is evidence to support that the consistent use of these agents in the care of patients with AD can prolong the time to flare, reduce the amount of topical corticosteroids used, and decrease the number of eczema flares.[1] Yet, when it comes to the prevention of AD, results from the Barrier Enhancement for Eczema Prevention (BEEP) trial did not show that use of moisturizers during the first year of life prevented the development of eczema in infants at high risk.[2]

Still, moisturizers play an important role in every AD patient's basic skin care routine. Bathing and use of moisturizers can help improve dry skin in AD. Seems simple, right? Yet, when it comes to bathing, why is the dogma that "bathing less frequently is better in AD" still widely believed? Primary care medicine is usually the first point of contact for most patients with AD, and some have theorized that it is the lack of awareness with respect to this issue that allows this dogma to persist among primary care providers. But articles from the American Academy of Pediatrics and the American Academy of Family Physicians reference the most current guidelines from the American Academy of Dermatology on the care of patients with AD, including bathing practices. However, a study examining publications of clinical practice patterns and how these align with current clinical guidelines for AD found that these are often not in complete sync.[3] The authors further hypothesized that this discrepancy may in part be driven by medical training, individual experience, and institutional "norms" that allow well-established opinions to persist. As former trainees, we are all well aware that our knowledge comes not only from books or other forms of texts but from the experience of our teachers and mentors who guide us throughout our years of training and beyond. While we should not discount the immense value that comes from learning from the experience of others, we should always remain inquisitive and question well-established dogmas, particularly when intuition argues against it.

1. Cochrane Database Syst Rev. 2017 Feb 6;2(2):CD012119.
2. Lancet. 2020 Mar 21;395(10228):962-72.
3. Dermatol Ther (Heidelb). 2018 Sep;8(3):349-77.

For clinicians who treat patients with atopic dermatitis

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Reference: 1. Bieber T. Interleukin-13: targeting an underestimated cytokine in atopic dermatitis. *Allergy*. 2020;75(1):54-62.

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