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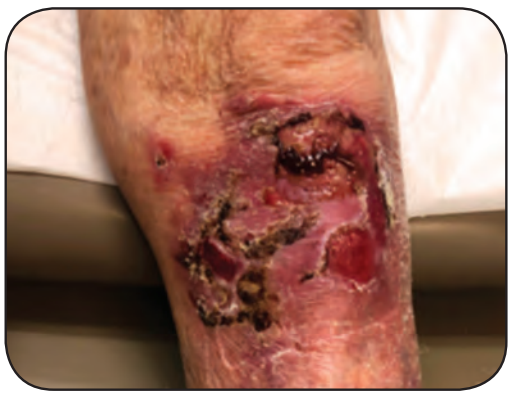
JDPA

Journal of Dermatology for Physician Assistants



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CALENDAR OF EVENTS

ALERT: Due to the coronavirus (COVID-19) pandemic, many medical organizations have made the difficult decision to cancel or postpone planned live events. Please refer to meeting host websites for more information.

SDPA Annual Summer Dermatology Conference
A Hybrid Conference Experience
July 22-25, 2021
Chicago Marriott Downtown Magnificent Mile
Chicago, Illinois
https://www.sdpaconferences.org/

Summer2021
AAD 2021 Summer Meeting
August 5-8, 2021
Tampa, Florida
https://www.aad.org/

Georgia Dermatology Physician Assistants
Dermatology Pearls CME Conference
September 9-11, 2021
The InterContinental Buckhead
Atlanta, Georgia
https://www.gadermpa.org

Pennsylvania Dermatology Physician Assistants (PDPA)
2nd Annual Keystone Dermatology CME Conference
October 15-16, 2021
The Logan Hotel
Philadelphia, Pennsylvania
http://www.padermpa.org/keystone-derm-2021.html

SDPA Annual Fall Dermatology Conference
November 4-7, 2021
InterContinental Hotel
Los Angeles, California
https://www.dermpa.org

FROM THE PRESIDENT'S DESK:

Teamwork is the Only Way

Dear Readers,

I must admit the last year and a half really tested my spirit. My outlook had been the lowest that I can remember, but one thing kept me going—teamwork! I have been in SDPA Leadership since 2012 and have built strong, lasting relationships with people I now consider my "SDPA family." With all the uncertainty, changes, and fears we have endured during the pandemic; I was at my limit. Our own losses, whether it was a family member, friend, job, or sense of stability and security, might have brought us to the brink of losing hope; but we were there for each other.

Being a valued team member is important not only in leadership but also in your personal and professional lives as well. We are all creatures of habit and believe things should be only one way, but we also must respect one another, think outside of the box, get out of our comfort zone, and just try to be a better human. Take the competitive nature out of your soul and cheer for each other. Give people the opportunity for growth and even teach them what they could do better. Support changes that come your way because, without change, there is no progress. In the end, we all want to be better than we were yesterday and have hope for the future. We all learn from our mistakes and can pass that wisdom on with a smile and encouragement.

Compassion is another important aspect of being part of a team. We all must take turns listening and being listened to. A good case example of conveying compassion and empathy can be seen when caring for a patient with neurotic behaviors such as excoriation disorder (also referred to as chronic skin-picking or dermatillomania), a mental illness related to obsessive-compulsive disorder. If you really listen to the patient, in the end, it has nothing to do with their skin, really, but a psychiatric, repetitive self-inflicting habit. The mind is a powerful tool, and it is guided by what you keep telling yourself is the truth. So, take that deeper dive and attempt to understand another person's point of view.

Speaking of point of view, it's equally important to be mindful of your own perspective and the attitude (verbal or nonverbal) you exude. Take for instance how you handle the reality of aging. You have a choice to be negative or positive about the aging process. Do you want to be that negative, grumpy individual that nobody wants to be around or the person who keeps positive and is a pleasure to have as company because they make you smile? A good mood is contagious and are good deeds, which can spark change in others. The beginning of any change typically has a very long story behind it.

Finally, I want to discuss the rule of acceptance. Sometimes, things do not go as planned. Okay, it may seem like this happens more than "sometimes," but who is counting? Every individual has their own opinions and many times, these might not jive with your own. A great example is when a patient seeks a "second opinion" as he or she may not agree with your diagnosis. Incongruence in opinion between care provider and patient isn't unusual and can happen for many reasons. Perhaps the patient is in denial that something could be wrong or maybe you did misdiagnose something (yes, it can happen). In the long run, healthcare is a team approach to achieve one common goal—to help and care for the patient.

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Instead of taking it personally that the patient might seek a second opinion, take the advice from above and tap into your positive, compassionate side to better understand and respect that individual's point of view.

The bottom line is this: As healthcare professionals, it is our duty to keep our patients safe and informed. We provide our wealth of knowledge to the people who need it; whatever they do with that knowledge is their prerogative. In the end, it is not solely our opinion that puts a patient on their path to healing, but rather our sharing of knowledge acquired through formal education and professional experience. The desire to better our patient care through knowledge sharing is a driving force behind SDPA's strength and success. That is why the SDPA consistently strives to offer stellar educational opportunities. That is why the SDPA membership is more than 4,000 strong and leading the Dermatology PA profession forward and making a difference. However, we cannot do it alone. It is not only made up of a stellar staff, but volunteers! Yes, all that you see happening in front of you is because of them. ALL OF IT! So, as I begin my term as SDPA President, I would like to ask you the following: "What are you doing for your profession?" What are you doing to make it better? Whether it is an hour a week or more, lending your time and talents can really make a difference. Ultimately, it is all about TEAMWORK and we need you!

I ask you to open your arms, embrace one another so that we may listen and learn as part of team. Also, let's work to embrace diversity and change—it is the only way forward to growth. While thinking about change, I'm reminded of a powerful and inspirational quote:

"The most dangerous phrase in our language is 'we've always done it this way.'"

- Grace Hopper, American computer scientist and first woman to hold the rank of Rear Admiral in the United States Navy.

Warm regards,

Renata Block

Renata Block, MMS, PA-C
President SDPA

Bullous Pemphigoid: Diagnosis, Treatment, and Management

By Lauren Hartman, DMSc, PA-C; Cynthia Faires Griffith, MPAS, PA-C; and Loderick A. Matthews, BS

ABSTRACT

Bullous pemphigoid, a rare autoimmune chronic skin disorder characterized by blistering, urticarial lesions (hives), and itching, is the most common among all pemphigoid diseases. BP has been growing in prevalence over the past two decades primarily due to an increasing elderly patient population and exposure to certain medication classes, such as dipeptidyl peptidase-IV (DDP-IV) inhibitors or "gliptins," that are associated with bullous pemphigoid onset. Both of these factors contributing to a rise in potential BP cases underscores the need for health care providers in dermatology to be familiar with the clinical presentation, causes, diagnostic tools, and treatments for this condition. This article describes clinical manifestations, causes, diagnostic work-up, and treatment for BP, and includes an patient vignette to further illustrate disease presentation and management

KEYWORDS

bullous pemphigoid, itching, urticaria, blistering, wound care

INTRODUCTION

Bullous pemphigoid (BP) is a rare autoimmune chronic skin disorder characterized by blistering, urticarial lesions (hives), and itching. BP is the most common among all pemphigoid diseases with a reported incidence of 10 cases per million population (pmp) per year in the United States (US).[1,2] BP, traditionally considered a disease of the elderly, mainly affects the patient population over the age of 60, however, it can appear earlier in life, including during infancy and childhood. Although classified as a rare condition, BP has been growing in prevalence over the past two decades, underscoring the need for health care providers to be aware and well equipped to care for these patients.[3]

PATHOPHYSIOLOGY & CLINICAL PRESENTATION

BP results from the autoimmune response to two proteins within the dermal-epidermal junction—BP180 and/or BP230 within the hemidesmosomes. Hemidesmosomes hold basal keratinocyte cells to the dermis. As a result, tense blisters form as the epidermal skin cells separate from the dermis. Prior to development of the blisters, itching can be present.[4]

In some patients, itching and urticaria can be the prodrome before the blisters; in other patients, pruritus can be the only presenting symptom with blisters never developing, making it a challenge to properly diagnose on visual examination alone. BP can be localized to one body surface area, typically the lower legs/feet, or generalized, and typical locations for BP reported in

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Approval is valid for 1 year from the issue date of August 3, 2021. Participants may submit the self-assessment exam at any time during that period.

This program was planned in accordance with AAPA's CME Standards for Enduring Material Programs and for Commercial Support of Enduring Material Programs. SDPA members may access the post-test at https://www.dermpa.org/JDPA_Exams

Learning Objectives:

1. *Discuss the pathophysiology and clinical manifestation of bullous pemphigoid,*
2. *Identify risk factors of bullous pemphigoid.*
3. *Discuss bullous pemphigoid prevalence and prognosis.*
4. *Review diagnostic tools to employ when bullous pemphigoid is suspected.*
5. *Review treatment modalities available and considerations, such as patient lifestyle, list of medications, and severity of disease in choosing a treatment plan for a patient with bullous pemphigoid.*

the literature are the trunk and extremities. Though the disease primarily affects the skin, 10 to 40 percent of patients experience mucous membrane involvement in the oral, ocular, and genital areas.[5,6]

RISK FACTORS & RELAPSE

Known risk factors of BP include genetic predisposition, age, adverse responses to medication, infections, and physical and viral agents.[1] Researchers have pointed to two main factors contributing to increased BP prevalence worldwide: 1) a growing elderly population with several comorbidities, such as type 2 diabetes mellitus (T2DM), cardiovascular diseases, and neurogenerative diseases and 2) environmental influences, such as UV radiation, traumas, and increased exposure to drugs that may potentially trigger the disease.[3] Age is a significant risk factor. Mean age of BP diagnosis ranges from 65 to 80 years with incidence exponentially increasing after age 70. Patients 90 and older have a 300-fold higher relative risk than those 60 or younger.[3,5,6,7]

Drug-induced BP cases have also been reported with certain medications triggering onset of disease.5 Drug types and examples associated with BP emergence include the following:

- **Dipeptidyl peptidase-IV (DDP-IV) inhibitors or "gliptins"** (e.g., vildagliptin and linagliptin) used to treat type 2 diabetes mellitus [T2DM])
- **Diuretics** (e.g., furosemide, spironolactone)
- **Antipsychotics** (e.g., phenothiazines with aliphatic side chain)
- **Cancer immunotherapies** (e.g., pembrolizumab, nivolumab, and durvalumab, all "checkpoint inhibitors" that target the programmed cell death protein-1 [PD-1] and the programmed death ligand-1 [PD-L1]

BP is a chronic, relapsing skin disorder that may be fatal, particularly in elderly, immunosuppressed patients who are at greater risk of succumbing to related side effects from dementia, infection, and sepsis, which have all been shown to be significant contributors to death in patients with BP.[8] Though patients can experience remission of disease with treatment, the relapse rate is high. Wang et al[9] conducted a systematic review to investigate relapse and risk factors for relapse in patients with BP reported in the literature. In their study, relapse, also referred to as a "flare," was defined using the following criteria: the appearance of at least three new lesions in one month (including blisters, urticarial plaques or eczematous lesions) or no less than one large (>10 cm in diameter) urticarial plaque or eczematous lesion that does not heal within one week, or the extension of original lesions or daily pruritus in patients within disease control. They concluded that the one-year relapse rate in patients with was more than 50 percent (range: 27.87-53%) after disease remission with the majority of relapse episodes occurring within six months during remission.[9]

DIAGNOSIS & TREATMENT

Although there are no widely accepted guidelines on diagnosis and management of BP, dermatology associations around the globe have put forth proposed criteria. There are currently multiple diagnostic tools for care providers who suspect BP, and diagnosis relies on careful examination of medical history, including a list of current and previous medications, clinical presentation, and histopathology. Four significant clinical predictors proposed by the French Bullous Study Group and adopted by other BP researchers include the following: 1) absence of atrophic scars, 2) absence of head and neck involvement, 3) absence of mucosal involvement, and 4) age greater than 70 years.[10] The authors showed that, if three of these four characteristics were present in a patient, a diagnosis of BP could be made with a sensitivity of 90 percent and a specificity of 83 percent.

Biopsy for histopathology should be taken from an intact bulla (using shave or punch technique) or punch biopsy from the edge of an erosion. Tissues samples are then placed in formalin and the pathologist examines the level of the skin that is separating to cause the blister formation; in the case of BP, this will be a subepidermal blister. Histology also elucidates the cell types present in the skin including lymphocytes, neutrophils, and eosinophils.

A biopsy of perilesional skin, meaning normal appearing skin that is within 1 cm of the blister, can be sampled with punch biopsy and placed in Michel's media for direct immunofluorescence testing. This testing looks for autoantibodies and other immunoreactants in skin to identify the type and where they are deposited within the skin. The patient's skin is cross sectioned and examined for in situ deposits of IgG, IgA, IgM, C3, and fibrinogen. Deposits of IgG or C3 in the basement membrane zone, or more specifically on the epidermal side of the blister, supports the diagnoses of bullous pemphigoid. Other blistering disease can present with different deposits in different locations. For example, IgA in the dermal papillae is characteristic of dermatitis herpetiformis.

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CLINICAL VIGNETTE –

An 82-year-old man was referred to dermatology outpatient clinic for nonhealing wounds on the lower legs. The patient had a medical history of chronic kidney disease stage 3, hypertension, gout, type 2 diabetes mellitus (T2DM), depression, and vitamin D deficiency. He also had a history of skin shearing trauma as a result of repeated falls on the left lower leg for the past three years. He has had home health/wound care for the past three years, treating wounds on his lower legs with Xeroform® and Hydrofera Blue® dressings. He also regularly wrapped compression bandages on the lower legs as part of the wound care routine but, two weeks prior to presentation at dermatology, "took a break" from using the compression bandages. Since making this change in his routine, he noticed the appearance of new blisters filled with clear fluid located under the skin on the left lower leg and left tibial tuberosity, which were all areas of previous trauma. He reported no history of blisters on the feet, right leg, arms, or scalp. The patient denied experiencing itching, malodorous drainage, or pain and did not have a history of similar blistering.

The patient's list of current medications included dulaglutide, hydralazine, insulin, levothyroxine, and losartan. Physical examination revealed erosions on the left tibial tuberosity with some erosions on an erythematous base. Of note, these erosions did not appear undermined. *Figure 1* shows the patient's left lower leg and left tibial tuberosity with chronic erosions and ulcers with granulation tissue. Unrelated to the leg erosions, the patient had an abrasion on the right vertex of the scalp and left arm from involvement in a car accident four days before his appointment.

A punch biopsy for histopathology was taken from the edge of the erosion on the left leg. *(Figure 2)*. A shave biopsy for histopathology was performed to remove a 4x5 mm bulla on an erythematous base; the entire bulla was shave biopsied *(Figure 3)*. Normal appearing skin within 1 cm of the bulla was punch biopsied for direct immunofluorescence. The patient's serum (blood) was taken for indirect immunofluorescence for autoantibodies against skin and enzyme-linked immunosorbent assays (ELISA). The histopathology from the punch biopsy of the erosion and the shave biopsy of the bulla showed a sub-epidermal vesicle with an inflammatory infiltrate of eosinophils, neutrophils, and lymphocytes. Type IV collagen was on the floor of the blister.

The perilesional skin punch biopsied for direct immunofluorescence revealed Immunoglobulin G (IgG), third component of complement (C3), and fibrin in the epidermal basement membrane *(Figure 4)*. The patient's serum tested for indirect immunofluorescence was positive for autoantibodies against the epidermal side of 1 M NaCl

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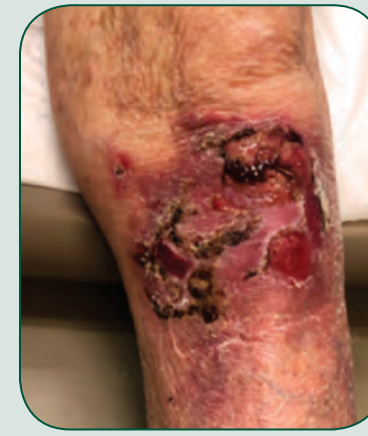

Figure 1.
Left leg with localized erosions, eschar, granulation tissue, and erythema

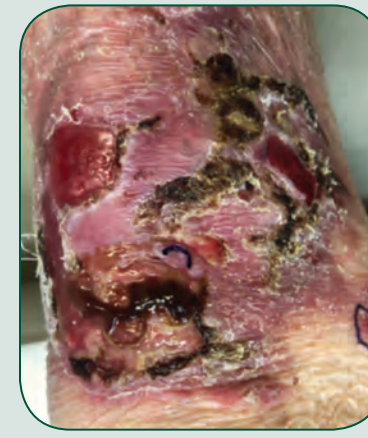

Figure 2.
Left leg with erosions, eschar, and erythema. The circled site at the edge of an erosion was punch biopsied for histopathology.

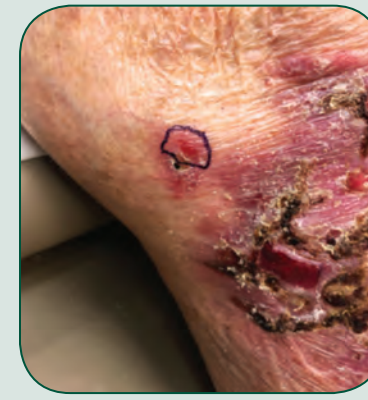

Figure 3.
Circled biopsy site on the left lateral leg denotes the site of shave biopsy of an intact bulla for histopathology.

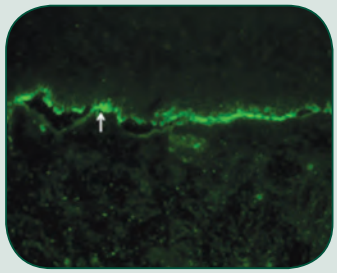

Figure 4.
Direct Immuno–fluorescence of 1 M NaCl split patient skin showing IgG localized to the epidermal side of the split.

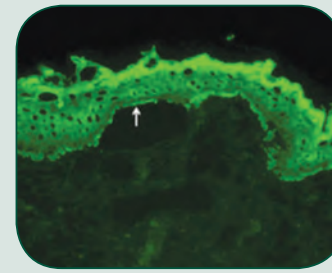

Figure 5.
Indirect Immuno–fluorescence of 1 M NaCl split foreskin showing IgG localized to the epidermal side of the split at a titer of ≥40.

split skin at a titer of ≥40 *(Figure 5)*. The patient's serum was then tested for IgG autoantibodies against baculovirus-derived BP180 and BP230 by ELISA. The patient was negative for IgG autoantibodies against both BP180 and BP230.

The patient's clinical picture and biopsy and direct and indirect immunofluorescence are compatible with the diagnosis of bullous pemphigoid (BP).

This patient was prescribed topical clobetasol to use on the left knee. He used this not on the open skin but on intact skin. As he had traumatic skin erosions from falls, the knee was covered with wound dressing with Vaseline then nonstick pad and then coban wrap. Care was taken to not shear off the tops of the blisters that developed with his dressing changes. The bullae healed with a little milia formation within three weeks of this treatment *(Figure 6)*. Since then, the patient was started on doxycycline and nicotinamide. He did not develop any new bullae. He did not tolerate the doxycycline due to gastrointestinal upset, so this was held. At the time of publication, the patient continued to have no new bullae.

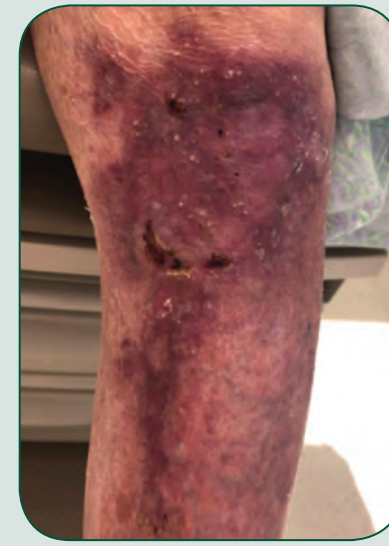

Figure 6.
Patient's leg after three weeks of topical steroid treatment, note the milia.

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Further tests that can be done to gain additional evidence for a diagnosis of BP is indirect immunofluorescence testing (IDIF) and enzyme-linked immunosorbent assays (ELISA). IDIF can be used to see if the patient's blood carries autoantibodies, specifically IgG, that localizes to the epidermal side of 1 M NaCl split skin, which could suggest that the IgG autoantibodies are binding to the hemidesmosomes (180 and 230) and causing the blistering. To further illuminate the target of the binding of the patient's autoantibodies, the serum is tested by ELISA. In ELISA, the patient's serum is diluted in a buffer, incubated in a well of a plate that is coated with the antigen of interest, BP180 or BP230 in this case, washed extensively and an enzyme conjugated antihuman IgG antibody is applied and incubated. After further washing, the enzyme substrate is added to the plate and if the patient's autoantibodies have bound the antigen, a color change is observed. This color change is read by a plate reader that measures the absorbance of transmitted light and produces a readout that can be quantified against the standards provided by the kit manufacturer. It's important to note that, when testing for BP, clinicians should look at the full clinical picture, not just a single test, which can potentially come out negative even though the diagnosis is in fact BP.

The goal of treatment for patients with bullous pemphigoid is to maintain complete resolution of existing lesions as well as prevent new flare-ups.[11] The current standard of care includes the use of systemic glucocorticoids (e.g., prednisone or prednisolone) and potent topical corticosteroids (e.g., clobetasol propionate). A study by Grantham et al compared the effects of oral doxycycline and oral prednisolone in treating BP.[12] This study ultimately found that prednisolone is not superior to doxycycline for treatment based on a six-week short term trial on blisters and life-threatening events for patients. Doxycycline has also been proven to be a safer long-term option, showing a decreased number of deaths caused by BP at a significantly greater rate compared with oral prednisolone.[12]

Combination treatments have also been described. For instance, using oral corticosteroids prior to use of doxycycline with doxycycline then used for additional maintenance has been shown to produce better control of the disease process. Ultimately, published literature supports the use of both modalities, with the final decision belonging to the medical provider who can determine the best treatment option for each patient on a case-by-case basis. Other medications have however led to some resolution of symptoms for BP. These include intravenous immunoglobulin therapy, which is beneficial for patients that are resistant to corticosteroids, as well as the monoclonal antibody drug rituxan, both of which have been studied for potential usage in improving this disease process.

Kremer et al discuss how bullous pemphigoid is often associated with morbidity and can affect an individual's overall quality of life.[3] Although systemic glucocorticoids are considered the hallmark medication for this condition, the long-term side effects associated with corticosteroid use (e.g., weight gain, hypertension, osteonecrosis, osteoporosis, insulin resistance, myopathy, cataracts, and glaucoma) are important to monitor. It is also vital that clinicians explore the use of other therapies, including rituximab and omalizumab, given that the safety profiles of these medications are considered superior to immunosuppressive agents such as azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, and cyclophosphamide. Rituximab is used to treat B-Lymphocyte related malignancies and was approved by the food and drug administration (FDA) in June of 2018 for treating pemphigus. The complete response rate for patients with rituximab was 85 percent.[3]

Omalizumab is used to treat chronic urticaria and has been shown to be beneficial in treating pemphigoid due to the role the drug plays in the release of Ig-E mediated histamine.[3] The complete response rate for patients with omalizumab was 84 percent. The recurrence rate for bullous pemphigoid was significantly lower with rituximab at 29 percent than omalizumab at 80 percent. The mean time to recurrence for rituximab was 10.2 months versus 3.4 months for omalizumab. Overall, rituximab established a lower recurrence rate and longer duration between recurrences.[3] Miyamoto et al[5] discusses various treatment modalities centered on enabling cutaneous healing while also gaining control of pruritus. A Cochrane systemic review published in 2010 analyzed ten randomized clinical trials based on the treatment modalities for BP. First-line recommendations include high-potency topical steroids such as clobetasol cream for mild-to-moderate severity and a systemic steroid such as prednisone for moderate-to-severe severity. The second-line treatments for mild-to-moderate disease include doxycycline and dapsone. For moderate-to-severe disease states, methotrexate, azathioprine, and mycophenolate mofetil are recommended. For severe cases intravenous immunoglobulin, rituximab and omalizumab are recommended. The aforementioned studies addressed overall improvement with topical corticosteroids, doxycycline, prednisone, rituximab, and omalizumab.[5] Combination therapies can improve the quality of life for a patient without impairing the comorbidities.

Immunosuppressive medications such as azathioprine, mycophenolate mofetil, and methotrexate can also be used as viable treatment options. Biologics ultimately selectively surpass the auto-antibody formation which prevents the inflammatory cascade, leading to a positive therapeutic outlook for patients. Reports have shown that methotrexate has a strong efficacy long term when analyzing the clinical remission of the disease process. The medications are particularly chosen based on their side effect profiles.

Ultimately, the evidence suggests the use of various modalities in treating this condition, thus treatment plans are often tailored to an individual patient's lifestyle, health, and preferences. For instance, if the disease is localized to an area, topical treatment with high-potency topical steroids like clobetasol would be a good option. If the patient has extensive disease covering more body surface area, other treatments like antibiotics, specifically doxycycline in combination with nicotinamide, also known as niacinamide or vitamin B3, can be utilized to slow the formation of additional bullae. Oral steroids are a mainstay of therapy if topical therapy is not feasible given body surface involvement; however, this can be detrimental to patient's bone and cardiovascular health when used long term, so steroid-sparing agents like azathioprine, mycophenolate, or rituximab are also used in refractory BP to arrest development of bullae.

CONCLUSION

BP is a chronic, relapsing skin disorder that may be fatal, particularly in elderly, immunosuppressed patients who are at greater risk of succumbing to related side effects from dementia, infection, and sepsis, which have all been shown to be significant contributors to death in patients with BP.[8] Though patients can experience remission of disease with treatment, the relapse rate is high. Diagnosis can be confirmed by looking at the full clinical picture comprising review of patient profile and medical history, visual examination, and histology. The

goal of treatment for patients with bullous pemphigoid is to maintain complete resolution of existing lesions as well as prevent new flare-ups. Evidence suggests the use of various modalities in treating this condition, thus treatment plans are often tailored to an individual patient's lifestyle, health, and preferences. With prevalence of BP on the rise globally, so too are the chances that dermatology providers will encounter a patient with BP. Becoming familiar with the manifestations, causes, diagnostic tools, and treatments discussed in a growing body of literature will ultimately facilitate better care for this condition.

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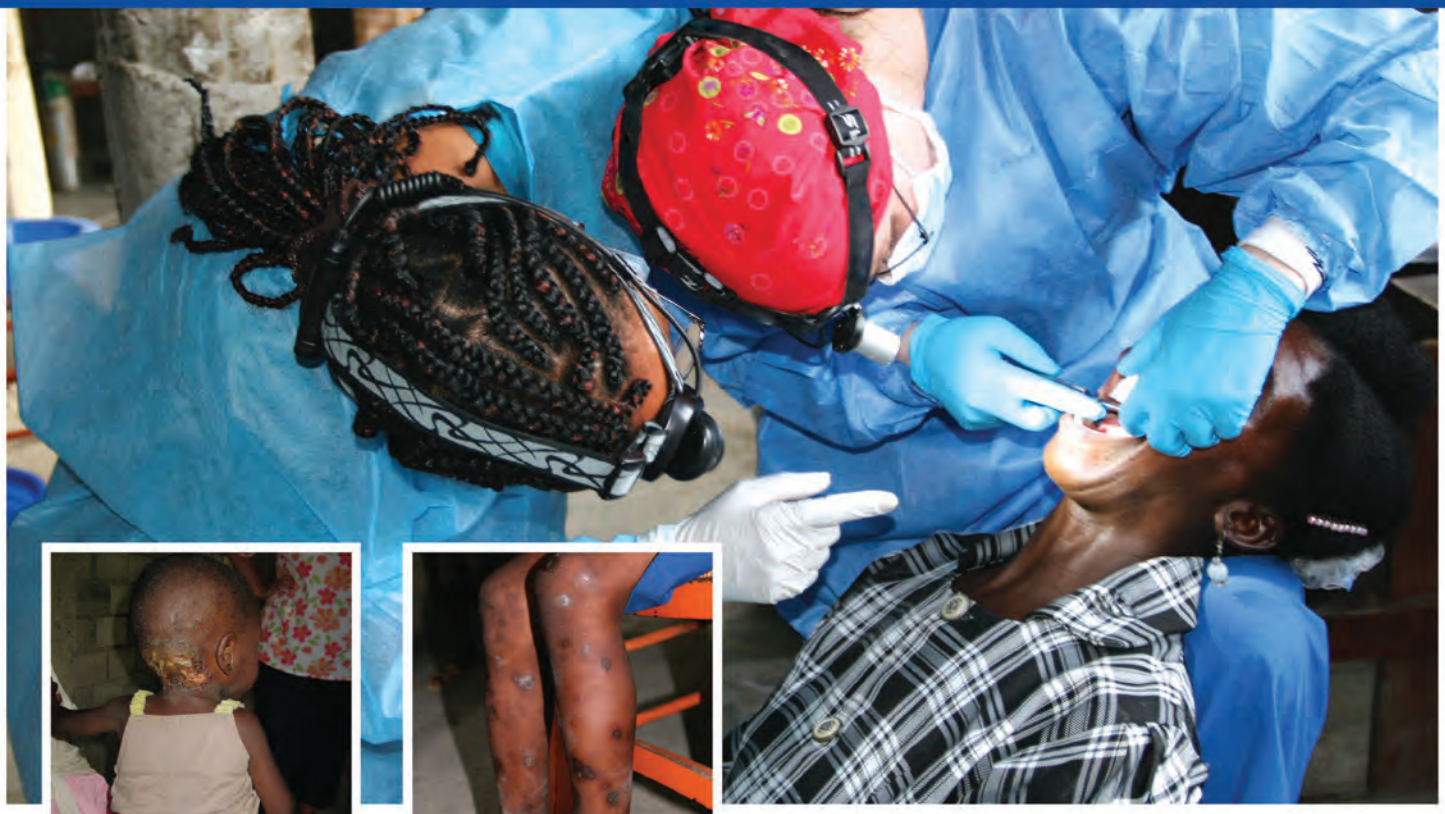

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Atopic Eruption of Pregnancy: A Case Report and Brief Topic Overview

By Peter A. Young, MPAS, and Lia C. Keller, MD, FAAD

ABSTRACT

Pruritus is a common symptom during pregnancy and can manifest as a result of multiple conditions. Atopic eruption of pregnancy is the most common dermatosis specific to pregnancy and does not represent a threat to the health of mother or fetus. However, other similar-appearing dermatoses of pregnancy can result in fetal harm or sub-optimal outcomes, hence these must be ruled out in the pruritic pregnant patient. Herein we present a case of atopic eruption of pregnancy and discuss the diagnostic approach to these patients.

KEYWORDS

Atopic eruption of pregnancy, specific dermatoses of pregnancy, pruritus in pregnancy, pemphigoid gestationis, polymorphic eruption of pregnancy, intrahepatic cholestasis of pregnancy.

INTRODUCTION

Atopic eruption of pregnancy (AEP) is an umbrella term created in 2006, which encompasses the older terms eczema in pregnancy, prurigo of pregnancy, and pruritic folliculitis of pregnancy. This updated phrase was part of a revision to the hallmark 1983 classification scheme created by Holmes and Black, which first defined the specific dermatoses of pregnancy as a group of pruritic skin conditions occurring uniquely in gravid women.[1,2] The most common dermatosis of pregnancy, AEP is characterized by a pruritic morbilliform eruption equally affecting the trunk and extremities with onset before the third trimester (incidence: 75%, mean: 18+9 weeks). Patients often present with numerous excoriations due to severe pruritus. Although most diagnosed with AEP have some atopic tendencies, only 20 percent have pre-existing atopic dermatitis. A correct diagnosis is important to ensure health of the fetus.[1-3]

CASE PRESENTATION

A 33-year-old woman, 25 weeks pregnant with her second child, was referred to dermatology for itching and what she described as hives on her extremities, abdomen, and lower back, ongoing since week 15 of her pregnancy. She had failed to respond to wet wraps with mupirocin and fluocinonide cream 0.05% twice daily for two

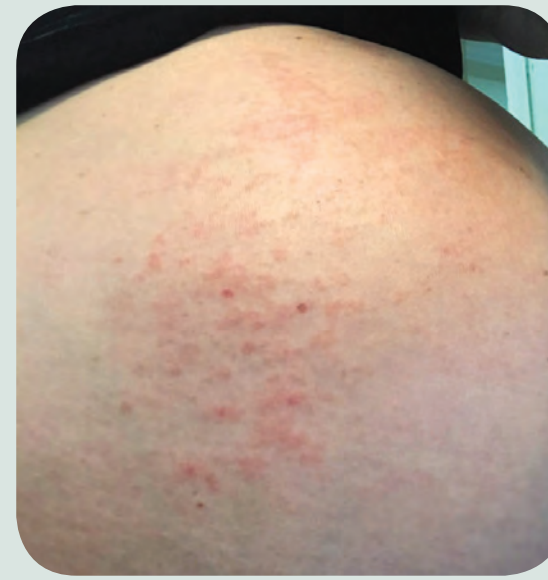

Figure 1: *Numerous erythematous edematous papules coalescing on the right lateral abdomen, with multiple small angulated red crusts.*

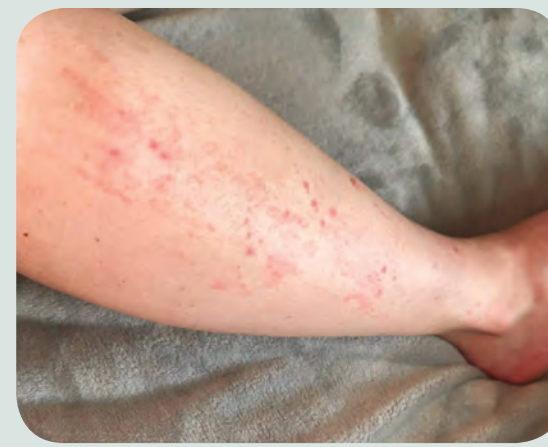

Figure 2: *Numerous erythematous papules and linear patches suggestive of excoriation on the right lower leg.*

weeks (recommended by her primary physician). Her history included eczema, epilepsy, and attention deficit hyperactivity disorder.

Exam revealed erythematous thin papules and angulated red crusts on the patient's bilateral ankles, lower legs, left thigh, lower back, and abdomen *(Figures 1 and 2).* Her serum alanine transaminase and bilirubin (total and direct) were normal. Punch biopsy of her left thigh revealed perivascular mixed inflammatory dermatitis with eosinophils, without marked spongiosis or papillary dermal edema. Our dermatopathologist's microscopic differential diagnosis included urticarial hypersensitivity reaction and pruritic urticarial papules and plaques of pregnancy (PUPPP).

Treatment was started with topical clobetasol 0.05% ointment twice daily, cetirizine 10 mg each morning, and diphenhydramine (25-50 mg each evening). She was encouraged to apply ice packs to itchy areas in lieu of scratching. The patient went on to deliver her child without complications via cesarean section at 39 weeks gestational age, with subsequent resolution of her dermatitis.

DISCUSSION

AEP's hypothesized pathogenesis is rooted in the mother's immune adaptations, requisite to tolerate her (antigenically different) in utero child. During pregnancy, maternal Th1 cytokine production and cell-mediated functions are downregulated, and Th2 cytokines and humoral response are increased. As a Th2-dominant disease, atopic diathesis may be "unmasked" in this immunologic setting, manifesting AEP as a result.[1]

A pregnant woman with pruritus and skin lesions requires urgent evaluation to ensure health of the fetus. Atopic eruption of pregnancy must be differentiated from polymorphic eruption of pregnancy (PEP, formerly called PUPPP), intrahepatic cholestasis of pregnancy (ICP), and pemphigoid gestationis (PG) formerly called herpes gestationis. In all four, severe pruritus is the main symptom. Although not itself associated with fetal risk, differentiating AEP from these is important: ICP can result in prematurity, fetal distress, and stillbirth, and PG. Where the pregnant pruritic woman presents with acute onset of pruritus during pregnancy and only secondary skin changes, ICP should be suspected, and serum bile acids checked. Where primary lesions are vesicles and bullae appearing in the third trimester, PG should be suspected, and a perilesional biopsy sent for direct immunofluorescence.[1,3]

In our case the lack of marked spongiosis or papillary dermal edema made the urticarial stage of pemphigoid gestationis unlikely, hence the primary differential diagnosis was PEP, polymorphic eruption, which can be relatively challenging to tell apart from AEP compared with the other specific dermatoses of pregnancy. Fortunately distinguishing these two can be a primarily academic exercise: they are managed similarly, neither threatens fetal health, and both improve or resolve postpartum.[3] Since biopsy findings of AEP and PEP can be nonspecific, and the terminology for specific dermatoses of pregnancy was revised in 2006 (recently enough to be after many currently practicing dermatopathologists completed their fellowships), the clinician may have to employ clinicopathologic correlation "outside the box" of what suggested diagnoses are listed on the pathology report. Based on our patient's atopic diathesis, onset prior to third trimester, characteristic primary lesion morphology, and classic distribution on the extremities, we categorized the patient as having AEP rather than PEP.

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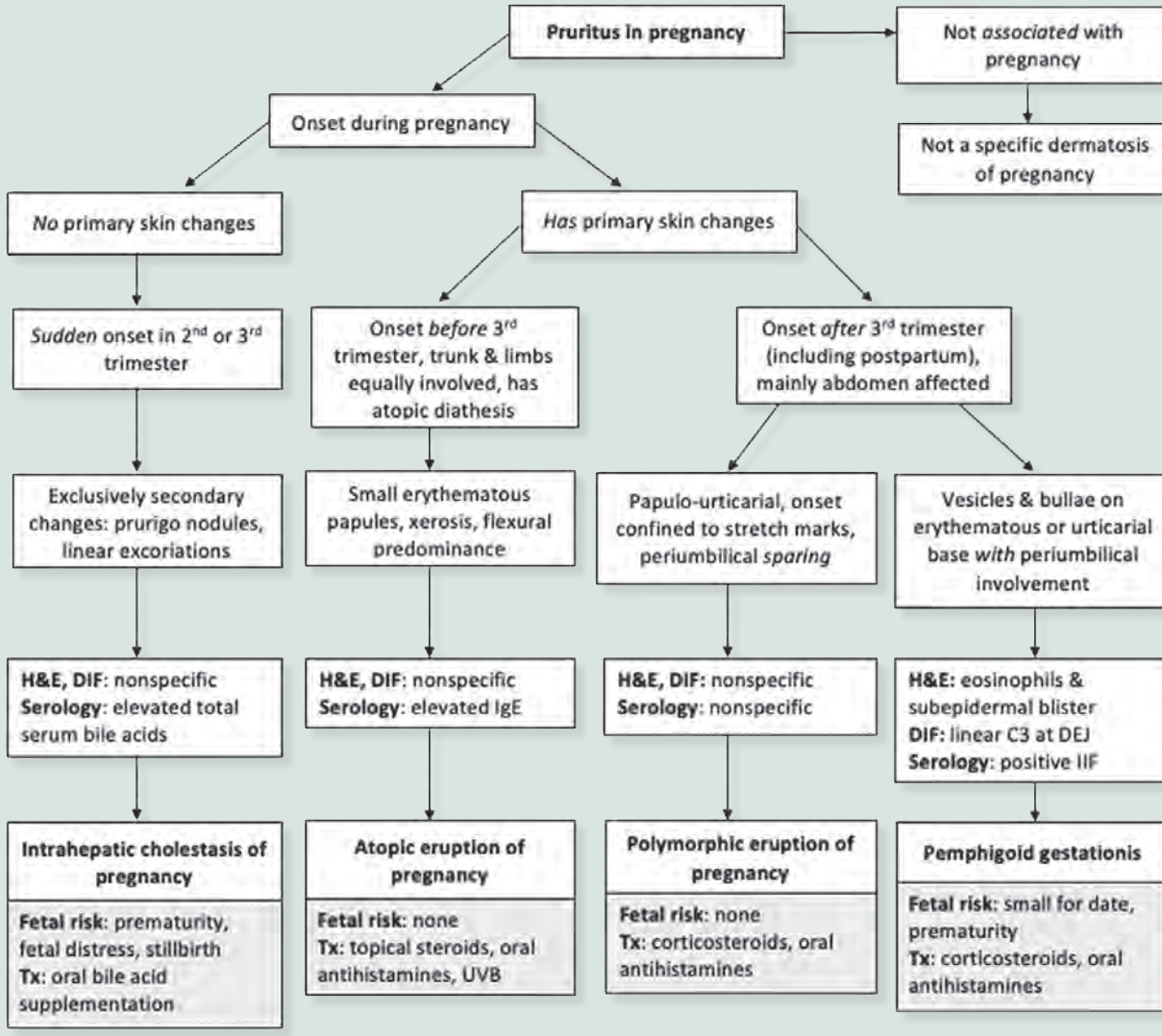
See page 18 for a summative diagram of the specific dermatoses of pregnancy, optimized for easy in-clinic reference when evaluating these patients.

DIAGNOSTIC ALGORITHM FOR PRURITUS IN PREGNANCY



Adapted from Ambros-Rudolph C, Mullegger R, Vaughan-Jones S, Kerl H, and Black MM. The specific dermatoses of pregnancy revisited and reclassified: Results of a retrospective two-center study on 505 pregnant patients. *J Am Acad Dermatol.* 2006 Mar;54(3):395-404. PMID: 16488288.

Abbreviations used: H&E, hematoxylin & eosin; DIF, direct immunofluorescence; DEJ, dermoepidermal junction; IIF, indirect immunofluorescence; Tx, treatment.

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On Individualized Eczema Care: No Two Patients Are Alike

By Steve Nelson

This article is the first in a series provided by the National Eczema Association.

ABSTRACT

More than 31 million Americans live with eczema, and yet the condition affects every person differently. The disease is complex and heterogeneous: every patient has a unique interplay of triggers, symptoms, comorbidities, and disrupted lifestyle. Given these variables, healthcare providers can benefit from hearing the individual experiences and concerns of their patients with eczema as they determine an appropriate and more personalized treatment plan. Eczema usually begins in infancy or childhood, but it can develop any time in a person's life. Symptoms can vary greatly across different demographic groups. The severity of eczema ranges from mild, to moderate, to severe. Three essential diagnostic criteria to determine the severity of a patient's condition include: the amount of body surface area affected, intensity of flares and frequency of flares. Chronic itchy skin is a universal symptom of most types of eczema. Caregivers of children with eczema carry a significant burden, reporting frustration, anxiety, sleeplessness, and "desperation" while trying to manage their child's symptoms. Many people with eczema share a common hope when choosing a treatment: immediate and sustained relief from itch. Designing the perfect treatment plan starts with listening to the patient's unique experience, concerns, and treatment preferences, from which a discussion about the available and appropriate options can occur. Through the process of shared decision making, the patient and healthcare provider, working together, can best customize a solution that meets each individual patient's or caregiver's needs.

KEYWORDS

Eczema, atopic dermatitis, shared decision making, dupilumab, burden of disease

INTRODUCTION

More than 31 million Americans live with eczema, and yet the condition affects every person differently. The disease is complex and heterogeneous: every patient has a unique interplay of triggers, symptoms, comorbidities, and disrupted lifestyle. Given these variables, healthcare providers can benefit from hearing the individual experiences and concerns of their patients with eczema as they determine an appropriate and more personalized treatment plan.

> *Many people with eczema share a common hope when choosing a treatment — immediate and sustained relief from itch.*
>
> *Here are some quotes from real patients:*
>
> *"My primary quality of life issue is itch. It's the itch that drives me crazy."*
>
> *"I just want to not itch."*
>
> *"Please focus on helping us reduce the itch as that's where it all starts."*

As the largest patient advocacy organization serving those who live with eczema and those who care for them, the National Eczema Association (NEA) collects, interprets, and distributes patient-reported data and insights that increase awareness of the patient's individual experience with the disease. In 2019, NEA co-hosted the landmark Patient-Focused Drug Development (PFDD) meeting for eczema where insights on the lived experience from patient and caregiver panels, as well as a survey administered prior to the meeting, were shared directly with representatives of the United States Food and Drug Administration (FDA), drug manufacturers, and other key stakeholders highlighting the burden of disease and implications of managing and treating eczema. The key findings and patient perspectives were published in the More Than Skin Deep Report, many of which are cited in this article; NEA also conducts regular surveys of the eczema community and select findings of that research is also included here.

AGE OF DIAGNOSIS, SYMPTOMS, AND PREVALENCE

Eczema usually begins in infancy or childhood, but it can develop any time in a person's life. Symptoms look different in infants and toddlers than in older children. With infants, early signs of the disease usually appear on the face, cheeks, chin, forehead, and scalp. As babies with eczema start crawling, symptoms can also appear on their elbows and knees. Eczema is also common in adults over the age of 60, with research into the adult onset of eczema on the rise. Skin can become drier and thinner as patients age, leaving the skin barrier less robust and more susceptible to environmental triggers.[1]

> *"There are nights I've slept in the same bed as him," she said. "I rub and scratch gently for him. If I don't, he can—and he literally will—tear himself apart."*
>
> *-Sarah Pry, parent of a child with eczema, explaining how caring for her son impacted her sleep patterns.*

Symptoms can vary greatly across different demographic groups. In patients with lighter skin, eczema often appears as a red, itchy rash or dry, scaly patches on the skin; in patients of color, eczema can look darker brown, purple, or ashen grey in color. In the United States, atopic dermatitis (AD) affects a greater percentage of Black children and White children compared to Hispanic children,[2-4] whereas Black and Hispanic children tend to have more severe AD compared to White children.[5]

SEVERITY OF DISEASE

The severity of eczema ranges from mild, to moderate, to severe. Three essential diagnostic criteria to determine the severity of a patient's condition include: the amount of body surface area affected, intensity of flares and frequency of flares. Alex Lumsden, a college freshman, described his mild-to-moderate eczema as "somewhat uncomfortable," with a rash on his neck, arms, and legs. However, over time Alex's condition progressed and became severe. "I don't want to move in the morning," he said, "because my entire face and arms are caked in dead skin cells and pus that has risen at night."[6] Lindsay J., in describing her own severe eczema, said that she would wake up "unconsciously clawing at [her] skin." Additional patient-reported symptoms of severe eczema may include blood-stained clothing or sheets, shame, disrupted personal relationships, negative self-image, anxiety, depression, and suicidal thoughts. Eczema can affect mental health incrementally, as well: healthcare providers can include mental health screening as a preventative practice in eczema management, even in the absence of any patient-reported mental health symptoms.

BURDEN OF DISEASE

Chronic itchy skin is a universal symptom of most types of eczema. A recent survey of adults with moderate to severe AD found that 70.5 percent of respondents reported severe, unbearable itch in the past two weeks; 85.8 percent reported daily itch; and 62.8 percent reported itching at least 12 hours per day.[7] Patients also report skin pain, with 33 percent of adults with AD reporting weekly pain and 5.2 percent reporting daily pain because of their AD.[8]

Sleep disturbance is also widely reported: 15 to 30 percent of adults with AD experience sleep-related issues including insomnia, daytime sleepiness, and fatigue, and rate sleep disturbance as the 'most' or 'second-most' burdensome symptom.[9] Sarah Pry explained how caring for her son impacted her sleep patterns. "There are nights I've slept in the same bed as him," she said. "I rub and scratch gently for him. If I don't, he can—and he literally will—tear himself apart."

Additional burdens that patients and caregivers report include the following:

- financial costs
- lost time at work
- hospitalization due to infection
- delays in education
- loss of friendships
- complications with physical intimacy
- emotional and mental exhaustion from the chronic nature of the disease.

CAREGIVERS AND ECZEMA

Caregivers of children with eczema carry a significant burden, reporting frustration, anxiety, sleeplessness, and "desperation" while trying to manage their child's symptoms. "This was not how we envisioned life as new parents," said Joseph Cutaran, father of two young children with eczema. Caregivers of children with eczema reported higher rates of sleep disturbance (48%) than adults with eczema (22%).[6] Keri Kelley said, "Living with eczema means calling the pediatrician at 3:00 a.m., begging for a sedative just to let [her son] get some sleep."

Caregivers also reported helplessness, disappointment, and guilt for not being able to help their children. Sarah Pry said that her son "has not had, and possibly never will have, the childhood that [she] had wished for him."

ECZEMA AND COMORBIDITIES

Diagnosed comorbidities are common across all demographics of people with eczema. Children with AD typically develop other atopic conditions in a sequence including food allergies, allergic rhinitis, and asthma–a progression known as the atopic march.[10] Mental health comorbidities are also widespread in patients with eczema. Children and adolescents with AD are 2 to 6 times more likely to have depression, anxiety, or attention deficit hyperactivity disorder than children without AD.[11,12] Ashley Ellis explained that her daughter Hadley's anxiety increased so much when she flared that she "stopped eating at school" and that it eventually progressed to "full panic attacks."[6] Adults with AD have a two-and-a-half to three-fold higher risk for anxiety or depression that increases with disease severity,[13] and rates of suicidal ideation are 44 percent more likely in people with AD.[14]

CARE AND TREATMENT

Many people with eczema share a common hope when choosing a treatment: immediate and sustained relief from itch. Lisa Choy, eczema patient and NEA board member, said, "My primary quality of life issue is itch. It's the itch that drives me crazy." Alison Piluso agreed: "I just want to not itch." And Stephen Gawron focused on itch, as well: "Please focus on helping us reduce the itch as that's where it all starts."

The challenge and opportunity for patients—and their healthcare providers—is collaborating on the right treatment for each individual. For example, patients report that affordability is a critical component in making a treatment plan work for them, so an open dialogue and exchange of information may best inform an optimal treatment plan. NEA's recent Out of Pocket Survey revealed that "48.6 percent of AD patient and caregiver respondents had OOP costs for prescriptions not covered by their insurance.[15] Additionally, patients at the PFDD meeting used words like "convenient," "safe," and "easy to obtain" when describing their ideal treatment. Other patients expressed their desire to see more treatments that focused on the underlying biology of the skin.

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The Saga of the Modifier 25

By Jaci J. Kipreos, CPC, CPMA, CDEO, CEMC, COC, CPCI

Introduction

Welcome to Compliance Corner, a new department dedicated to providing information and tools to help keep your healthcare documentation for coding and billing compliant. This new resource aims to help you navigate recent changes to Current Procedural Terminology® (CPT®) Evaluation and Management (E/M) guidelines for office visits, which became effective January 1, 2021. Written by the American Medical Association (AMA), these guidelines contain new methodology and new definitions, both of which affect the way you as providers document the account of the patient visit.

As is often the case with significant change, attempts to comprehend and adapt to new guidelines has set off a chain reaction of follow-up questions. Here, we will provide clinical examples to assist in the explanation of these new requirements to support the different levels of service of CPT office visit codes. We will also feature YOUR questions on all compliance-related topics along with answers that walk you through the rationale for each response. Compliance Corner will contain a selection Q&As from you, the readership. If you have a scenario or question, we encourage you to send it to coding@dermpa.org for review.

I'm excited to bring you the second installment of Compliance Corner in which we will discuss what I believe to be one of the hottest topics surrounding coding—the Modifier 25.

There has been so much hype around this one single modifier that one would think it is associated with high-dollar scenarios, however it is often not associated with big ticket items. So, why all the hype? Why all this attention placed on one little modifier?

To explain the hype, we need to look at this topic from some different perspectives. First, we need to consider what the AMA had in mind when the modifier was created. We must also consider what payers expect from this modifier and what it means to potential payments. Then, we have to consider regulations and policy and documentation.

The Intent of the Modifier – The AMA Perspective

Let's begin with defining the purpose of the CPT manual. The AMA created CPT as a way to conveniently relay information to insurance carriers. The CPT manual is just a description of work. The code descriptions and information do not guarantee payment. The intent is to just describe work.

Modifiers were created by the AMA to assist in describing situations where there is a possibility of nonpayment because the coding would appear to describe a scenario that would not fall into the "typical" scenario. Realistically speaking, once a claim for services reflects more than one CPT code, there is a consideration of whether a modifier is needed. An office visit reported with a lab or an x-ray would not normally necessitate the need for a modifier; however, try to report an office visit and a minor procedure together without a modifier and chances are the claim may be denied or one of those charges will not be paid. The Modifier 25 was created to address this exact scenario. The CPT manual describes the Modifier 25 as a way to convey to a payer that the work involved in the office visit was separate from the work performed in the procedure. Here is an excerpt from the CPT manual on Modifier 25:

Modifier 25

Significant, Separately Identifiable Evaluation and Management Service by the Same Physician or Other Qualified Health Care Professional on the Same Day of the Procedure or Other Service. *It may be necessary to indicate that on the day a procedure or service identified by a CPT code was performed, the patient's condition required a significant separately identifiable E/M service above and beyond the other service provided or beyond the usual preoperative and postoperative care associated with the procedure that was performed. A significant separately identifiable E/M service is defined or substantiated by documentation that satisfies the relevant criteria for the respective E/M service to be reported. The service may be prompted by the symptom or condition for which the procedure and/or service was provided. As such, different diagnoses are not required for reporting of the E/M services on the same date. This circumstance may be reported*

by adding modifier 25 to the appropriate level of E/M service.

Note: this modifier is not used to report a service that resulted in a decision to perform surgery. See modifier 57.

This description by the AMA provides an overview, yet it does still leave some openings based on interpretation. Phrasing such as "significant separately identifiable" leaves some room for interpretation. For example, one might question what is meant by "usual preoperative and postoperative." Every surgical CPT code that is reported includes in its value the work of the associated preoperative and postoperative services.

Pre-work is considered site assessment, decision to perform the procedure, informed consent, obtaining information about allergies, obtaining information about immunization status, if relevant.

Post-work includes post procedural instructions.

Note that the separate evaluation of a condition is NOT included. The definition of the modifier indicates that the medical documentation should clearly show that the E/M service performed was unique and distinct from the usual preoperative and postoperative care associated with the primary procedure performed on the same date of service. The definition indicates that the patient's condition required this additional work beyond the typical pre- and post-operative care provided.

What Do Payers Want?

This is where the definition begins to get a bit confusing. Various commercial payers may have their own policies based on their interpretation of the modifier. Always check in with your billing department to understand the policies of commercial plans.

For the purposes of this article, it is best to address how Medicare interprets this modifier and what the documentation should reflect. The Centers for Medicare and Medicaid Services (CMS) provides manuals that describe how to use the modifiers and instructs their contracted payers how to reimburse if the modifier is submitted appended to an E/M code.

The Medicare Claims Processing Manual Chapter 12 indicates the following instructions concerning payment for minor procedures when reported with an E/M service:

40.1.C. Minor Surgeries and Endoscopies.

Visits by the same physician on the same day as a minor surgery or endoscopy are included in the payment for the procedure, unless a significant, separately identifiable service is also performed. For example, a visit on the same day could be properly billed in addition to suturing a scalp wound if a full neurological examination is made for a patient with head trauma. Billing for a visit would not be appropriate if the physician only identified the need for sutures and confirmed allergy and immunization status.

Medicare contracts with other payers to handle the Medicare claims submitted in various geographical regions. These contractors, known as Medicare Administrative Contractors or MACs, also provide instructions for payment. See Table 1 for examples of MACs and their guidelines on billing with Modifier 25.

Who Else Cares?

This modifier has caused so much attention from payers and providers that the Office of Inspector General (OIG) has decided to get involved. The OIG has as one of its goals to fight fraud, waste, and abuse. The OIG establishes and publishes a Work Plan that outlines areas of interest that will be under investigation to determine if services rendered were actually performed and if payment should have been made. The Work Plan is an ongoing list of areas of concern that is continually updated on the OIG website (www.oig.hhs.gov). The OIG investigates payments associated with Medicare and Medicaid. Commercial payers will often perform investigations based on the OIG Work Plan.

This year, the OIG added the following item *(see Table 1)* to their Work Plan:

The OIG described their reasoning as follows:

Medicare covers an Evaluation and Management (E/M) service when the service is reasonable and necessary for the diagnosis or treatment of illness or injury, or to improve the functioning of a malformed body member. Generally, Medicare payments for global surgery procedures include payments for necessary preoperative and postoperative services related to surgery when furnished by a surgeon. Medicare global surgery rules define the rules for reporting E/M services with minor surgery and other procedures covered by these rules. ***In general, E/M services provided on the same day of***

...Continued on page 27

TABLE 1. Dermatology-related audit update initiated April 2021 in the Office of Inspector General's Work Plan

Announced	Agency	Title	Component	Report Number
April 2021	Centers for Medicare and Medicaid Services	Dermatologist Claims for Evaluation and Management Services on the Same Day as Minor Surgical Procedures	Office of Audit Services	W-00-21-35868

TABLE 2. Medicare Administrative Contractors Guidelines on Billing with Modifier 25.

NOVITAS SOLUTIONS, INC.

Representing: AR, CO, LA, MS, NM, OK, TX, Indian Health and Veteran Affairs

Modifier 25 Tips for Use:

Question: Why is the patient being seen? Are there signs, symptoms, and/or conditions the physician or the other qualified health care professional must address before deciding to perform a procedure or service?

If answered "YES," based on the documentation, an E/M service might be medically necessary with modifier 25.

If answered "NO," based on the documentation, an E/M service might NOT be medically necessary with modifier 25.

- **Example:** An established patient was scheduled for a follow up E/M. The physician met the documentation requirements for a 99213. The patient then complained that he was washing dishes, dropped a glass and now his thigh muscle felt like a piece of glass went through his skin. Based on the signs and symptoms documented, the physician performed 20520 (removal of foreign body in muscle or tendon sheath; simple), which has 10 global days. **The proper billing would be 99213 25 and 20520.**

Question: Were the physician's or other qualified health care professional's evaluation and management of the problem significant and beyond the normal preoperative and postoperative work?

If answered "YES," an E/M may be billed with modifier 25.

If answered "NO," it is NOT appropriate to bill with modifier 25.

- **Example:** An established patient sustained a severe laceration to the scalp. Before suturing the laceration, the physician performed and documented a comprehensive history and exam to determine if the patient sustained neurological damage. The physician then performed a 3.0 cm intermediate repair (12032) to the scalp. Based on the signs, symptoms, and conditions documented, the physician went above and beyond the normal preoperative work. **The proper billing would be procedure code 12032 and the appropriate level of E/M service and append the modifier 25.**

NORIDIAN JURISDICTION E

Representing: CA, HI, NV, American Samoa, Guam, Northern Marian Islands

Modifier 25 Statements:

- To bill for an E/M service, must have a history, exam, and medical decision making (HEM). All procedures include some service related to patient evaluation and management. A separate E/M should include its own HEM. Physician must determine whether problem is significant enough to require additional work to perform key components of problem-oriented E/M service.
- Do not append to E/M codes that are explicitly for new patient only (CPTs 92002, 92004, 99201-99205, 99321-99323, and 99341-99345). These codes are listed as new patient codes and are automatically excluded from global surgery package edit. They are reimbursed separately from surgical procedure and no modifier is required if visit meets significant and separately identifiable guidelines.
- Do not use when documentation shows amount of work performed is consistent with that normally performed with procedure.

Palmetto GBA JM

Representing: NC, SC, VA, WV

Example of Incorrect Use of CPT Modifier 25:

- **Scenario:** An E/M service is submitted with CPT code 99213 and CPT modifier 25 and procedure code 11042. During the same patient encounter, the physician also debrides the skin and subcutaneous tissues (CPT code 11042, 0 global days). CPT 99213 was submitted to reflect the physician's time, examination, and decision-making related to determining the need for skin debridement. The physician's time was not significant and separately identifiable from the usual work associated with the surgery, and no other conditions were addressed during the encounter.
- **Outcome:** Do not submit the E/M service. The E/M service is not separately reimbursable from the surgical procedure. Submit only the surgical procedure (CPT code 11042).

Example of Correct Use of CPT Modifier 25:

- **Scenario:** On January 3, an E/M service is submitted with CPT code 99214. The patient was scheduled to receive an injection into the left knee. Due to the failure to control pain and inflammation in the left osteoarthritic knee with prior medical treatments (oral meds and joint injections), further evaluation was performed by the physician and total knee replacement (TKR) of the left knee is planned.
- **Outcome:** Submit CPT modifier 25 with the visit for the evaluation and planned major surgery to treat the patient's arthritis.

...Continued from page 25

service as a minor surgical procedure are included in the payment for the procedure. The decision to perform a minor surgical procedure is included in the payment for a minor surgical procedure and must not be reported separately as an E/M service.

An E/M service should be billed only on the same day if a surgeon performs a significant and separately identifiable E/M service that is unrelated to the decision to perform a minor surgical procedure. In this instance, the provider should append a modifier 25 to the appropriate E/M code. In 2019, about 56 percent of dermatologists' claims with an E/M service also included minor surgical procedures (e.g., lesion removals, destructions, and biopsies) on the same day. This may indicate abuse whereby the provider used modifier 25 to bill Medicare for a significant and separately identifiable E/M service when only a minor surgical procedure and related preoperative and postoperative services are supported by the beneficiary's medical record. We will determine whether dermatologists' claims for E/M services on the same day of service as a minor surgical procedure complied with Medicare requirements.

Documentation

Reviewing these few examples, it is easy to understand the confusion in proper use and correct documentation to support the need for this modifier. The policies presented by payers are not specialty specific and that can create confusion on how to relate to the examples. The documentation must reflect work that is above and beyond just making the decision to perform the minor procedure. The documentation needs to reflect additional work and decisions concerning the condition or conditions.

The most typical scenario in dermatology will be the established patient who presents with a lesion and the decision is made to biopsy or destroy. Does the documentation reflect that the whole encounter was spent determining the need to perform the procedure? Or does the documentation reflect that the decision-making extended to counseling about the condition and explaining the nature of the condition? This is what a payer would want to read to consider payment for the visit and the procedure.

This has been a hot topic for many years and now that the OIG is involved, the stakes are even higher. Modifiers and coding which are a part of the business side of healthcare is a team effort. Communicate with your coders and billers. Ask questions about the different payer policies. This issue of the Modifier 25 definitely has the potential to impact the bottom line of the business. However, the ultimate questions to help guide coding compliance with Modifier 25 are as follows:

1. *Did you document to support the need for an additional service?*
2. *Was the work involved in the office visit beyond the typical preoperative work and postoperative work, and was it more than a work-up to determine the need for the procedure?*

Conclusion

In conclusion, the best defense is a good offense. Talk with your support team to determine specific payer policies that are unique to your geographic area. When documenting the events of the encounter, consider if the amount of work performed goes beyond the definition of "typical" pre-work and post-work of the procedure. Ask your team if your visits with a 25 modifier are being reimbursed. Lastly, always ask questions and be involved.

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Address for Correspondence: *If you have a question or comment, we encourage you to send it to coding@dermpa.org.*

Listening To Patients
Physician Extenders

By Alan Rockoff, MD

The following is an excerpt from Dr. Rockoff's third and most recent book titled "Doctoring from the Outside In: Dermatology Under the Skin."

Twenty-five years ago, a doctor I hardly knew called to ask a favor. The daughter of his friend was studying in Pennsylvania to be a physician assistant. He knew I hosted students. Could she shadow me for a couple of days? I was free and agreed.

At that point I had heard the term "physician assistant," but had no clear idea of what that label signified. During our three days together, I asked my guest what a physician assistant is allowed to do. "Pretty much everything," she said. "We have to work under a physician's supervision, but we can do that in any specialty."

This surprised me. After all, to become a physician requires four years of medical school, followed by a one-year internship. After that, doctors can be licensed, but almost every one of them signs on for several more years of training, even to become a primary physician. To be a certified as a physician assistant, by contrast, takes only two years after college. Was that really enough to work in "any specialty?"

I later learned that physician assistants began in the US Navy during World War II, when there were not enough fully trained doctors to provide medical services in emergency situations. After the war, continued shortages of medical personnel led to incorporating PAs into the medical workforce. The physician assistant world went on to develop its own infrastructure—a professional organization, publications, meetings, continuing education programs, recertification policies, and so forth.

The dynamic of PA professional development proceeded along the lines familiar to any profession: campaigns for greater scope of practice, developing specialties and subspecialties, a journal, job placement services. By the time I decided a few years later to engage the services of a PA in my own practice, I could turn to the Society of Dermatology Physician Assistants, a well-organized and efficient group with a fine hiring database. I engaged a physician assistant to work with me.

Fresh out of school, Kelly had no specific dermatologic experience beyond a few weeks of study during her training. Ironically, even this brief school-based exposure to dermatology exceeded my own in medical school. For a few months, Kelly followed me around like a student. After a few months she began to see patients on her own. We met regularly to review her medical management and office notes on patients she had seen. She brought any questions she had to my attention, and we went on meeting regularly.

At the start I wondered not only whether she would master the clinical craft but whether patients would accept her. The answer turned out to be a clear "yes" to both. Patients were of course informed they would be seeing a physician assistant. When Kelly married and left town three years later, some of the people she had worked with called to inquire whether it would now be acceptable if they saw me. I graciously agreed.

Over the next several years, I hired three cohorts of what these days are called "mid-level providers"—five physician assistants and one nurse practitioner. I trained them all from scratch. All were acceptable, several excellent, the last pair—PAs both—absolutely superb. We have been colleagues for well over a decade.

In recent years NPs and PAs have become more tightly and visibly integrated into the health-care landscape. Asked to identify their primary care provider, many patients answer along the lines of, "Officially, it's Dr. Osuna, but actually I see his nurse, Deb. She's terrific."

Patients expect to see such providers and accept them. Mid-level providers are now ubiquitous—in offices, clinics, and hospitals, often on the front lines of care, welcomed by patients and doctors, including this one, who speaks from personal collegial experience.

Having trained and worked beside physician assistants, I have seen the way they take on the challenge of daily clinical work—caring for ordinary people with everyday problems—with empathy and enthusiasm. It has been a pleasure to be their colleague. Our shared patients have thought so too for twenty years. The physician assistant who has worked beside me the longest, almost fifteen years, is the best colleague I ever had, and among the finest people I have ever met.

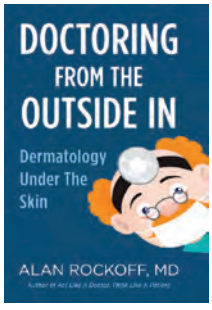
I am ambivalent about some of the changes my profession has undergone since I began.

Not this one.

Alan Rockoff, MD, *practices dermatology in Boston, Massachusetts. He graduated with his medical degree in 1972 from the Albert Einstein College of Medicine in Bronx, New York and then completed a pediatric internship and residency at Bronx Municipal Hospital Center in Bronx, New York. Continuing his education, Dr. Rockoff completed a dermatology residency program at the combined program at Boston University and Tufts University in Boston, Massachusetts.*

Dr. Rockoff is a Clinical Assistant Professor of Dermatology at Tufts University School of Medicine. He has taught senior medical students and other trainees for more than 35 years. Dr. Rockoff has been named one of Boston's Top Doctors by Boston Magazine for five years. Dr. Rockoff is board certified by the American Board of Pediatrics and the American Board of Dermatology. Dr. Rockoff is a Fellow of the American Academy of Dermatology and a member of the Massachusetts Medical Society and the Massachusetts Academy of Dermatology. Dr. Rockoff's publications have appeared in numerous journals. He writes a monthly column for his dermatologic colleagues in Dermatology News as well as a blog for the magazine Psychology Today.

His first book, "Under My Skin: A Dermatologist Looks at His Profession and His Patients" is available on Amazon and is his second book, "Act Like a Doctor, Think Like a Patient: Teaching Patient-focused Medicine" is available on Amazon and at Barnes and Noble. His third and most recent book, "Doctoring from the Outside in: Dermatology under the Skin" is available on Amazon in paperback and Kindle format.



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Dermatology Market Watch

Society for Immunotherapy of Cancer Publishes Clinical Practice Guideline on Immune Checkpoint Inhibitor-related Adverse Events

The Society for Immunotherapy of Cancer (SITC), the world's leading member-driven organization dedicated to improving cancer patient outcomes by advancing the science and application of cancer immunotherapy, is pleased to announce the publication of a clinical practice guideline focusing on management of the toxicities called immune-related adverse events (irAEs) that can affect cancer patients treated with immune checkpoint inhibitors (ICIs).

The "Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immune checkpoint inhibitor-related adverse events" published in the Journal for ImmunoTherapy of Cancer (JITC), was developed by an expert panel of leaders in immunotherapy as well as diverse subspecialties to provide recommendations on best practices for managing clinically relevant irAEs that arise during treatment with ICIs, including the common gastrointestinal, and dermatologic toxicities in addition to the more mare yet potentially serious neurologic and cardiac events, among other key considerations for oncologists treating their patients with these agents.

"Checkpoint inhibitors have transformed cancer care, yet these unique therapies can cause toxicities that are quite different than what is seen with traditional anti-cancer treatments and our understanding of irAEs is con," said Julie R. Brahmer, co-chair of the SITC Immune Checkpoint Inhibitor-related Adverse Events Expert Panel. "The Expert Panel considered the latest evidence available in the literature as well as their own vast wealth of experience in treating irAEs to develop this guideline, which will provide clinicians with the most current thinking on toxicity management, in order to safely use checkpoint inhibitors and provide the best-possible outcomes for patients."

ICIs are treatments that unleash the immune system against cancer, but the same mechanisms that underpin their effective anti-tumor properties may cause unique toxicities, specifically irAEs. As ICIs increasingly become integrated into treatment plans for an ever-increasing number of disease settings, there is a need for clear, expert guidance on the recognition and management of irAEs.

"I am pleased to share in the excitement of SITC's long-awaited clinical practice guideline on immune checkpoint inhibitor-related adverse events." said SITC President Patrick Hwu, MD. "The eleventh manuscript published in SITC's Cancer Immunotherapy Guidelines series, this guideline is critically important to oncologists in the management of these unexpected adverse events, and ensures the best possible outcomes for cancer patients receiving FDA-approved immunotherapies."

The SITC Cancer Immunotherapy Guidelines are a collection of clinical practice guidelines (CPGs) developed by leading experts to help hematologists and oncologists determine when and how to best use immunotherapy to treat their patients. The published disease-state specific guidelines provide evidence- and expert consensus-based recommendations on topics including selection of appropriate immunotherapy treatments, toxicity management, biomarkers, and considerations for patient quality of life. SITC has published CPGs for acute leukemia, bladder carcinoma, cutaneous melanoma, head and neck squamous cell carcinoma, immune checkpoint inhibitor-related adverse events, immune effector cell-related adverse events, lymphoma, multiple myeloma, non-small cell lung cancer, prostate cancer and renal cell carcinoma. Additional guidelines in development include those covering breast cancer, hepatocellular carcinoma, nonmelanoma skin cancer, as well as updates for the urothelial (bladder carcinoma) and lung cancer disease settings.

In addition to the published manuscript, SITC is also offering a number of different opportunities to help clinicians understand and implement the guidelines into their practice. One such resource are the live webinars and on-demand modules hosted on the SITC website. SITC will host live, free webinars during which attendees will be able to learn more about the recommendations included in this clinical practice guideline and ask questions of expert faculty, thus deepening their understanding of the concepts in the manuscript so they may feel comfortable safely administering cell therapies.

SITC is a proponent for collaboration and harmonization of efforts between like-minded organizations whenever possible. SITC thanks the American Society of Transplantation and Cellular Therapy (ASTCT) and all participating organizations for providing representatives to serve on SITC's Immune Checkpoint Inhibitor-Related Adverse Events Expert Panel and for their efforts in developing this clinical practice guideline.

To learn more about SITC and access available resources for clinicians on implementation of the new guidelines, visit https://www.sitcancer.org/research/cancer-immunotherapy-guidelines

Galderma Receives FDA Approval for Restylane® Contour for Cheek Augmentation and Correction of Midface Contour Deficiencies

Galderma's first and only product in the U.S. to use proprietary XpresHAn Technology™ for the cheeks

Galderma announced the U.S. Food and Drug Administration (FDA) has approved Restylane® Contour for cheek augmentation and correction of midface contour deficiencies in adults over the age of 21.[1] Restylane Contour, a new hyaluronic acid (HA) dermal filler, is Galderma's first and only product in the U.S. formulated with XpresHAn Technology™ for the cheeks. XpresHAn Technology™ uses a unique manufacturing process which creates a smooth, injectable gel that integrates into the skin for natural, dynamic expression in motion.[1-4]

Cheek filler searches have risen in popularity 218% from 2018-2020.[5] Restylane Contour provides a treatment with high patient* satisfaction.†

"Cheeks are the cornerstone of the face, and focusing on natural contour and not just volume loss can result in a dynamic expression that amplifies their natural beauty.[1,6]" said Dr. Leslie Baumann, MD, a board-certified dermatologist in Miami and a lead investigator in the clinical trial of Restylane Contour. "Hyaluronic acid levels in the skin diminish as we age, causing the face to lose shape, while increasing the likelihood that wrinkles and folds will appear."[7,8]

"In the past, it was all about volume for the cheeks, but consumers today are looking for natural-looking results, such as the dynamic expression provided by XpresHAn Technology™,[1-4]" said Diane Gomez-Thinnes, Head of Galderma U.S. "Developed by leading innovators in the hyaluronic acid filler market, Restylane Contour delivers a treatment you can trust. While individual results may vary, 98% of Restylane Contour patients* were pleased with their result at 1 year.[9]‡ The dynamic results truly speak for themselves."

The FDA approval of Restylane Contour is supported by data from a randomized, comparator-controlled, multi-center, pivotal Phase 3 study conducted at 15 centers across the United States.[9] The study evaluated 270 patients* across two groups over 48 weeks. Group A compared the effectiveness and safety of Restylane Contour (n=142) versus a control comparator (n=68). Group B compared the injection of Restylane Contour with needle (n=60) and cannula devices (n=60) in the same patient* on each side of their face. Results showed that Restylane Contour is safe and effective for cheek augmentation and the correction of midface contour deficiencies. Patients* treated with Restylane Contour required less total volume injected to achieve optimal aesthetic results§¶# compared to patients* treated with the comparator (4.26 mL versus 4.88 mL, respectively). In Group A, ≥76% of patients* treated with Restylane Contour were 'satisfied' with their cheeks compared to ≥73% treated with the comparator across all FACE-Q questions through Week 48.‡ Among patients* in Group B, more than 91% were "satisfied" with their cheeks across all FACE-Q questions at all timepoints through Week 48.†‡

In the Phase 3 study, Restylane Contour was well tolerated for cheek enhancement. The most commonly observed side effects for cheek injection were bruising, redness, swelling, pain, tenderness, and itching at the injection site. Most patients* (85%) did not experience any adverse events (AEs) related to treatment with Restylane Contour. There were no severe or late-onset AEs related to Restylane Contour treatment, and 93% of AEs related to treatment with Restylane Contour were mild in intensity (53/57), with four moderate AEs of bruising, pain and/or facial pain. Restylane Contour showed comparable efficacy and safety when injected with needles and cannula devices.[1,9]

Outside of the U.S., XpresHAn Technology™ is known as OBT and Restylane Contour is marketed as Restylane Volyme, which received its CE-mark in 2010 and has been used to treat over 1.5 million patients worldwide to date.[10]

Availability of Restylane Contour. Galderma will work closely with its aesthetic injector partners to introduce Restylane Contour in respective practice locations across the country beginning this summer.

To learn more about Restylane Contour, and review full Important Safety Information, visit RestylaneUSA.com.

About Galderma's Restylane Product Portfolio. The FDA approval of Restylane Contour adds to

*Patient=Clinical trial subject
† FACE-Q satisfaction with the cheek questionnaire
‡ FACE-Q rating of "very satisfied" or "somewhat satisfied" with questions
§ ≥1 grade improvement in midface fullness at 12 weeks
¶ MMVS (Medicis Midface Volume Scale)
# Post-hoc analysis data on the total amount of product needed to show an improvement in midface fullness 12 weeks after treatment

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INFORMATION FOR AUTHORS

JDPA
Journal of Dermatology for Physician Assistants

The official journal of the Society of Dermatology Physician Assistants

JOURNAL OVERVIEW

The *Journal of Dermatology for Physician Assistants* (*JDPA*) is a peer-reviewed publication that delivers innovative clinical, surgical, cosmetic, and professional content exclusively for dermatology PAs. Submissions to the *JDPA* are peer-reviewed by a panel of experienced dermatology PAs, educational PAs, and dermatologists before being accepted for publication. Manuscripts submitted for publication are reviewed with the understanding that they are original and have neither been submitted elsewhere nor are being considered by other journals. Electronic submissions are accepted and should be sent to jdpa@dermpa.org.

JDPA follows the recommendations of the International Committee of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), and the Committee on Publication Ethics (COPE) for guidance on policies and procedures related to publication ethics. The policies submission requirements listed in *JDPA*'s Author Guidelines have been adopted from those three advisory bodies and, where necessary, modified and tailored to meet the specific content, audiences, and aims of *JDPA*.

EDITORIAL MISSION

The *Journal of Dermatology for Physician Assistants* (*JDPA*) is the official clinical journal of the Society of Dermatology Physician Assistants. The mission of the *JDPA* is to improve dermatological patient care by publishing the most innovative, timely, practice-proven educational information available for the physician assistant profession.

Manuscripts that meet our editorial purpose include, but are not limited to, original research pertaining to the field of dermatology and/or physician assistant education and practice, review articles on dermatological conditions and their treatments, case reports and studies, clinical pearls related to surgical and/or cosmetic procedures, commentaries on published literature, opinion essays on current issues, and letters to the editor.

CONTENT FOCUS

The main departments featured in *JDPA* are as follows:

- Clinical Dermatology
- Cosmetic Dermatology
- Dermatology PA News & Notes
- Professional Development
- Surgical Dermatology

Dedicated departments may comprise features or regular columns that highlight content specific to their subject matter.

JOURNAL STYLE

All aspects of the manuscript, including the formatting of tables, illustrations, and references and grammar, punctuation, usage, and scientific writing style, should be prepared according to the most current *American Medical Association (AMA) Manual of Style* (http://www.amamanualofstyle.com)

Author Listing. All authors' names should be listed in their entirety and should include institutional/professional affiliations and degrees held.

Authoring Groups. If you choose to include an organization, committee, team, or any other group as part of your author list, you must include the names of the individuals as part of the Acknowledgments section of your manuscript. This section should appear after the main text prior to your References section. (If your Acknowledgments includes both group members and other persons/organizations who are not in that group, you should instead list the group members in a separate appendix to avoid confusion.) The terms "for" or "on behalf of" must also be used when referencing the authoring group in the by-line.

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Reference Formatting Guide

Journal article with 1 author
Zweibel K. Engineering. The impact of tellurium supply on cadmium telluride photovoltaics. *Science*. 2010;328(5979):699-701.

Journal article with more than 5 authors
Lim HW, Collins SAB, Resneck JS Jr, et al. The burden of skin disease in the United States. *J Am Acad Dermatol*. 2017 May;76(5):958-972.e2. Epub 2017 Mar 1.

Authored book
Griskey RG. *Transport Phenomena and Unit Operations*. Hoboken, NJ: John Wiley & Sons, Inc.; 2005.

Edited book
Cleophas TJ. *SPSS for Starters and 2nd Levelers*. 2nd ed. 2016. (Zwinderman AH, ed.). Cham: Springer International Publishing; 2016.

Book chapter
Worbs T, Förster R. T Cell Migration Dynamics Within Lymph Nodes During Steady State: An Overview of Extracellular and Intracellular Factors Influencing the Basal Intranodal T Cell Motility. In: Dustin M, McGavern D, eds. *Visualizing Immunity. Current Topics in Microbiology and Immunology*. Berlin, Heidelberg: Springer; 2009:71-105.

Website
Davis J. Soccer Players May Be At Risk Of Dementia From Repeatedly Heading The Ball. IFLScience. https://www.iflscience.com/health-and-medicine/soccer-players-may-be-at-risk-of-dementia-from-repeatedly-heading-the-ball/. Published February 15, 2017. Accessed October 30, 2018.

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- ***Continuing Education (CME).*** Content should be specific to the field of dermatology following any of the following formats: Original research (clinical or basic science), Professional issues or health policy papers, Scholarly review of a topic. **Recommended content length:** up to 5,000 words not including references. **Requirements:** Learning Objectives (4), Statement explaining how the article addresses practice gaps, and Self-assessment post-test questions (4).
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COSMETIC DERMATOLOGY

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- ***Cosmetic Pearls***. A brief article on a fact or pearl for the cosmetic setting (250-500 words).
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- ***Feature Articles***. A review of a new or innovative dermatological procedure, device, and/or approach to patient care (500-1000 words).
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- ***Surgical Dermatology Case Report.*** A report discussing a case(s) that illustrates an important or interesting observation (500-1500 words).
- ***Surgical Dermatology PA Perspectives.*** Write a review of published article summarizing the practical thoughts and clinical issues (250-1000 words).

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- All abbreviations and acronyms should be spelled out at first mention.

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Abstract. Include a structured abstract with all articles, except letters to the editors. Abstracts should be limited to 250 words and summarize the manuscript's main points (e.g., a research article might contain the following abstract categories: objective, design, setting, participants, measurements, results, conclusion.
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Supplemental Material. References to any online supplemental information must appear in the main article. Such supplemental information can include but are not limited to additional tables, figures, videos, audio files, slide shows, data sets (including qualitative data), and online appendices. If your study is based on a survey, consider submitting your survey instrument or the key questions as a data supplement. Authors are responsible for clearly labeling supplemental information and are accountable for its accuracy. Supplemental information will be peer reviewed, but not professionally copyedited.

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CONTENTS

Efficacy and Safety of Roflumilast Foam 0.3% in Patients with Seborrheic Dermatitis in a Randomized, Double-blind, Vehicle-controlled Phase 2 Study

Matthew Zirwas[1], Zoe D. Draelos[2], Janet DuBois[3], Leon Kircik[4], Angela Moore[5], Linda Stein Gold[6], Robert C. Higham[7], Lynn Navale[7], Patrick Burnett[7], David R. Berk[7]

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Introduction: Seborrheic dermatitis is a chronic inflammatory skin condition, which may cause physical discomfort and emotional burden for patients including itching, stress, and embarrassment. Topical treatments, such as antifungals, steroids, immunomodulators, and dandruff shampoos are used, but there is a need for efficacious and safe options, especially for long-term use. The objective of this study was to understand the efficacy, safety, and tolerability of once-daily treatment with roflumilast foam 0.3% for 8 weeks in patients with seborrheic dermatitis.

Methods: A phase 2, 8-week study investigated roflumilast foam 0.3%, a potent, phosphodiesterase-4 inhibitor designed for once-daily treatment of lesions on the scalp, face, and body. Patients with at least moderate severity (mean IGA 3.1) and mean BSA 3.2% were randomized to roflumilast foam 0.3% (n=154) or vehicle foam (n=72).

Results: For the primary endpoint, IGA success at Week 8, 73.8% and 40.9% patients achieved IGA of clear/almost clear in the roflumilast foam and vehicle groups, respectively ($P<0.0001$). Improvement in IGA success was statistically significant starting at first post-baseline visit (Week 2, $P=0.0033$) and continuing through Week 8 ($P<0.0001$). Scaling and erythema were both significantly reduced at Week 8 in patients on roflumilast foam compared to vehicle ($P\leq0.002$). Among patients with baseline Worst Itch Numeric Rating Scale (WI–NRS) score ≥4 (n=184/226), statistically significant 4-point reduction in WI-NRS was achieved as early as Week 2 with roflumilast foam compared to vehicle ($P\leq0.0007$). Rates of application-site pain, treatment-related adverse events, and discontinuations due to adverse events were low and comparable to vehicle.

Conclusions: Once-daily roflumilast foam 0.3% was safe, well tolerated, and effective in treating erythema, scaling, and itch of seborrheic dermatitis, and represents a promising and mechanistically novel treatment with early onset of action.

Long-term safety and efficacy of roflumilast cream 0.3% in adult patients with chronic plaque psoriasis: results from a 52-week, phase 2b open-label study

Linda Stein Gold,[1] Melinda J Gooderham,[2] Kim A Papp,[3] Laura K Ferris,[4] Mark Lebwohl,[5] David N Adam,[6] Javier Alonso-Llamazares,[7] H Chih-ho Hong,[8] Steven E Kempers,[9] Leon H Kircik,[5,10] Wei Jing Loo,[11] Walter K Nahm,[12] Daniel Stewart,[13] Matthew Zirwas,[14] Patrick Burnett,[15] Robert C Higham,[15] Lynn Navale,[15] David R Berk[15]

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Introduction: Roflumilast cream is a potent phosphodiesterase-4 inhibitor in development for plaque psoriasis. Favorable efficacy and safety of roflumilast cream in psoriasis from a phase 2b, 12-week study was recently published.[1] The objective of this study was to evaluate long-term (52 weeks) safety of once-daily roflumilast cream.

Methods: Patients from the phase 2b study could continue on open-label roflumilast cream 0.3% (Cohort-1, n=230) and patients naïve to roflumilast were enrolled (Cohort-2, n=102; NCT03764475). All psoriasis lesions (except scalp) were treated, including face and intertriginous areas.

Results: With cumulative treatment up to 64 weeks in Cohort-1 and 52 weeks in Cohort-2, long-term safety and tolerability were consistent with the 12-week, phase 2b study. Overall, 73.5% of patients completed the study; 3.9% discontinued due to adverse events (AE), and 0.9% due to lack of efficacy. Treatment-related AEs were reported in 2.7% of patients; none were serious AEs. Investigator tolerability assessments at each visit demonstrated 99% of patients rated no evidence of irritation. At Week 52, Investigator Global Assessment (IGA) of clear/almost clear and 2-grade improvement from baseline, was achieved by 34.8% of patients in Cohort-1 and 39.5% in Cohort-2. Of patients in Cohort-2, 40% of patients achieved IGA success at Week 12. Of patients receiving roflumilast cream 0.3% in the parent trial who achieved IGA of clear/almost clear at 12 weeks and continued in the open-label trial, 66.7% achieved IGA of clear/almost clear at 64 weeks or their last visit.

Conclusions: In this long-term safety study, roflumilast cream was well tolerated with no unexpected AEs, and effectively maintained clear/almost clear skin.

References: 1. Lebwohl MG, et al. *NEJM* 2020;383:229-39

Once-daily Roflumilast Foam 0.3% for Scalp and Body Psoriasis: A Randomized, Double-blind, Vehicle-controlled Phase 2b Study

Leon H Kircik[1], Angela Moore[2], Neal Bhatia[3], Alim R Devani[4], Zoe D Draelos[5], Janet DuBois[6], Melinda J

Gooderham[7], Steven E Kempers[8], Edward Lain[9], Mark Lee[10], Dedee F Murrell[11], Kim A Papp[12], David M Pariser[13], Rodney Sinclair[14], Matthew Zirwas[15], Patrick Burnett16, Robert C Higham[16], Lynn Navale[16], David R Berk[16]

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Introduction: Scalp psoriasis (S-PsO) affects 40% of patients either alone or in combination with body psoriasis. Associated itch, scale and social embarrassment adversely impact quality of life. Hair limits efficacy of creams and ointments and reduces treatment adherence, making treatment of S-PsO difficult. Roflumilast foam 0.3%, is a potent, nonsteroidal, phosphodiesterase-4 inhibitor for once-daily treatment of scalp, face, and body psoriasis. We investigated roflumilast foam for S-PsO and body PsO in a phase 2b randomized, double-blind, vehicle controlled 8-week study.

Methods: Patients ≥12 years old with at least mild disease (assessed separately for scalp and body) and ≤25% BSA were randomized to roflumilast foam (n=200) or vehicle (n=104).

Results: The primary endpoint of S-IGA success (clear/almost clear and ≥2-grade reduction from baseline) at Week 8 was achieved by 59.1% and 11.4% of patients receiving roflumilast foam and vehicle ($P<0.0001$), respectively; 34.3% and 3.4% rated clear at Week 8. Significant improvement occurred by Week 2. Body IGA success (clear/almost clear and ≥2-grade reduction from baseline) at Week 8 was achieved by 40.3% and 6.8% for roflumilast foam and vehicle ($P<0.0001$). Among the 88.5% of patients who reported Scalp Itch Numeric Rating Scale (SI-NRS) ≥4 at baseline, 71.0% and 18.5% who received roflumilast foam and vehicle, respectively, had ≥4-point improvement at Week 8 ($P<0.0001$). Roflumilast foam was well-tolerated. Treatment-related adverse events (AEs), application site AEs, and discontinuations due to AE were low and similar to vehicle.

Conclusions: Once-daily roflumilast foam improved both scalp and body PsO with improvement apparent as early as 2 weeks after treatment initiation.

Roflumilast cream, a once-daily, potent phosphodiesterase-4 inhibitor, in chronic plaque psoriasis patients: Efficacy and safety from DERMIS-1 and DERMIS-2 Phase 3 trials

Mark Lebwohl,[1] Leon H Kircik,[1,2] Angela Moore,[3] Linda Stein Gold,[4] Zoe D. Draelos,[5] Melinda J Gooderham,[6] Kim A Papp,[7] Jerry Bagel,[8] Neal Bhatia,[9] James Del Rosso,[10] Laura K Ferris,[11] Lawrence J Green,[12] Adelaide A Hebert,[13] Terry Jones,[14] Steven E Kempers,[15] David M Pariser,[16] Paul S Yamauchi,[17] Matthew Zirwas,[18] Patrick Burnett,[19] Robert C Higham,[19] Lynn Navale,[19] David R Berk[19]

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Introduction: Roflumilast 0.3% cream, a potent phosphodiesterase-4 inhibitor, may represent a highly effective, well-tolerated, nonsteroidal, once-daily treatment for long-term management of chronic plaque psoriasis, including the face and intertriginous areas. Two identical Phase 3, randomized, double-blind, vehicle-controlled, multi-center trials (DERMIS-1 [n=439; NCT04211363] and DERMIS-2 [n=442; NCT04211389]) were conducted in patients ≥2 years old with chronic plaque psoriasis.

Methods: Patients were randomized 2:1 to receive roflumilast cream 0.3% or vehicle once-daily for 8 weeks. The primary efficacy endpoint was Investigator Global Assessment (IGA) success at Week 8.

Results: Significantly more roflumilast-treated patients reached IGA success (DERMIS-1: 42.4%; DERMIS-2: 37.5%) than vehicle-treated patients (DERMIS-1: 6.1%; DERMIS-2: 6.9%, $P<0.001$). In patients with intertriginous area involvement, significantly more roflumilast-treated patients reached intertriginous-IGA (I-IGA) success at Week 8 than vehicle-treated (DERMIS-1: 71.2% vs. 13.8%, $P<0.0001$; DERMIS-2: 68.1% vs 18.5%, $P=0.0004$). Most of these patients achieved I-IGA=0. Approximately 40% of patients achieved 75% reduction in Psoriasis Area Severity Index by week 8 (DERMIS-1: 41.6% vs. 7.6%; DERMIS-2: 39.0% vs 5.3%, $P<0.0001$). Patients with baseline Worst Itch-Numeric Rating Scale (WI-NRS) ≥4 achieved a 4-point reduction in WI-NRS at Week 8 (DERMIS-1: 67.5% vs 26.8%; DERMIS-2: 69.4% vs 35.6%, $P<0.0001$). Itch improvement was notable by two weeks, the earliest timepoint measured (DERMIS-2: $P=0.0026$). Incidence of treatment-emergent adverse events (TEAE) were low and similar between roflumilast and vehicle

groups. Pooled rates of TEAE leading to discontinuation (roflumilast: 1.0%) and application site pain (roflumilast: 1.0%) were low and comparable to vehicle (1.3% and 0.3%, respectively).

Conclusions: Roflumilast cream 0.3% demonstrated favorable safety and tolerability while delivering statistically superior efficacy vs vehicle across multiple endpoints in patients with chronic plaque psoriasis.

Effisayil 1: A multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of spesolimab in patients with a generalized pustular psoriasis flare

Hervé Bachelez[1,2], Siew Eng Choon[3], Slaheddine Marrakchi[4], A. David Burden[5], Tsen-Fang Tsai[6], Akimichi Morita[7], Alexander A. Navarini[8], Min Zheng[9], Jinhua Xu[10], Hamida Turki[4], Milan J. Anadkat[11], Sushmita Rajeswari[12], Hairui Hua[13], Sebastian D. Vulcu[14], David Hall[12], Kay Tetzlaff[14,15], Christian Thoma[16], Mark G. Lebwohl[17]

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Introduction: IL-36 is central to the pathogenesis of generalized pustular psoriasis (GPP), an autoinflammatory disease characterized by widespread recurrent flares of sterile skin pustules ± systemic inflammation. No therapies for GPP flares are approved in the USA or Europe. A previous Phase I, open-label study of spesolimab, an anti-IL-36 receptor antibody, reported rapid pustule clearance in GPP patients.

Objectives: Efficacy and safety/tolerability of spesolimab from this first placebo-controlled trial in GPP patients are reported.

Methods: Effisayil 1 (NCT03782792) is a 12-week, double-blind, randomized, placebo-controlled Phase II study in patients with a GPP flare. Overall, 53 patients were randomized 2:1 to receive one 900 mg intravenous dose of spesolimab or placebo. The primary endpoint was a GPP Physician Global Assessment (GPPGA) pustulation subscore of 0 (pustule clearance) at Week 1. The key secondary endpoint was a GPPGA score of 0/1 (clear/almost clear) at Week 1. Other secondary endpoints were 75% improvement in Generalized Pustular Psoriasis Area and Severity Index (GPPASI) and pain visual analog scale (VAS). Safety endpoints included adverse events (AEs).

Results: A GPPGA pustulation subscore of 0 at Week 1 was achieved by 54.3% (19/35) of patients receiving spesolimab versus 5.6% (1/18) receiving placebo (one-sided p=0.0004). Results were sustained throughout the study. A GPPGA score of 0/1 at Week 1 occurred in 42.9% (15/35) of patients receiving spesolimab versus 11.1% (2/18) receiving placebo (one-sided p=0.012). At Week 4, 45.7% (16/35) of patients receiving spesolimab achieved 75% improvement in GPPASI versus 11.1% (2/18) receiving placebo (risk difference 34.6 [95% confidence interval 5.8–55.4]; one-sided p=0.008).

The spesolimab group reported greater improvement in pain VAS (p=0.001) at Week 4 versus the placebo group. Most AEs were mild/moderate and similar between study arms at Week 1.

Conclusions: IL-36 receptor inhibition with spesolimab demonstrated rapid and sustained improvements in GPP flares versus placebo, and favorable benefit–risk profile.

Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, Compared With Placebo and Apremilast in Moderate to Severe Plaque Psoriasis: Efficacy and Safety Results From the Phase 3 POETYK PSO-1 and POETYK PSO-2 Trials

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Introduction: Deucravacitinib is a novel, oral, selective inhibitor that achieves high selectivity by uniquely binding to the regulatory, versus active, domain of TYK2.[1] This study compared the efficacy and safety of deucravacitinib versus placebo and apremilast in two Phase 3 trials of plaque psoriasis.

Methods: Two double-blinded, 52-week trials (POETYK PSO-1, NCT03624127; POETYK PSO-2, NCT03611751) randomized patients (1:2:1) with moderate to severe plaque psoriasis to placebo, deucravacitinib 6 mg QD, or apremilast 30 mg BID. Patients receiving placebo switched to deucravacitinib at Week 16. Patients receiving apremilast who failed to meet trial-specific efficacy

thresholds (PASI 50, PSO-1; PASI 75, PSO-2) switched to deucravacitinib at Week 24. Coprimary endpoints were PASI 75 and sPGA 0/1 response versus placebo at Week 16. Key secondary endpoints included superiority versus placebo and apremilast.

Results: 666 and 1020 patients were randomized in PSO-1 and PSO-2, respectively. Demographic and baseline disease characteristics were balanced across groups. Greater proportions of patients in the deucravacitinib versus placebo and apremilast arms achieved PASI 75 (PSO-1: $P<0.0001$; PSO-2: $P\leq0.0003$) and sPGA 0/1 (both trials: $P<0.0001$) responses at Week 16. Deucravacitinib responses increased beyond Week 16 and were superior to apremilast at Week 24 in both trials (all $P<0.0001$). In both trials, >80% of deucravacitinib patients who achieved PASI 75 at Week 24 and continued treatment maintained PASI 75 response at Week 52. In PSO-2, median time to PASI 75 response loss was 85 days after deucravacitinib withdrawal at Week 24. During the placebo-controlled periods, the most common AEs (≥5% in any arm [pooled safety data]) were nasopharyngitis (8.6% [placebo]/9.0% [deucravacitinib]/8.8% [apremilast]), upper respiratory tract infection (4.1%/5.5%/4.0%), headache (4.5%/4.5%/10.7%), diarrhea (6.0%/4.4%/11.8%), and nausea (1.7%/1.7%/10.0%). Overall AEs, SAEs, and AEs leading to discontinuation were similar across groups. No clinically meaningful changes were observed in laboratory parameters over 52 weeks.

Conclusion: Deucravacitinib was superior to placebo and apremilast across efficacy endpoints and well tolerated in patients with psoriasis.

References: 1. Burke JR et al. *Sci Transl Med*. 2019;11:1-16.

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Efficacy of Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 Inhibitor, in Musculoskeletal Manifestations of Active Psoriatic Arthritis in a Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial

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Abstract:

Introduction: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates IL-23, IL-12, and interferon α/β signaling. Deucravacitinib, a novel, oral selective inhibitor of TYK2, acts via the TYK2 regulatory domain. Phase 2 results showed deucravacitinib was efficacious and well tolerated versus placebo (PBO) in patients with active psoriatic arthritis (PsA). This analysis further evaluated improvements in musculoskeletal disease manifestations in the Phase 2 PsA trial.

Methods: The one-year Phase 2 trial (NCT03881059) enrolled patients who had a PsA diagnosis for ≥6 months, met CASPAR criteria, had active disease (≥3 tender joints, ≥3 swollen joints, C reactive protein [CRP] ≥3 mg/L), and ≥1 active skin lesion. Patients failed or were intolerant to ≥1 NSAID, corticosteroid, csDMARD, and/or 1 TNF inhibitor (TNFi; ≤30%). Patients were randomized 1:1:1 to deucravacitinib 6 mg QD or 12 mg QD or PBO, and stratified by TNFi status (experienced vs naive) and body weight (<90 vs ≥90 kg). The primary endpoint, American College of Rheumatology (ACR) 20 response at Week 16, was met. The current prespecified subgroup analysis assessed achievement of ACR20 response at Week 16 based on study stratification factors. A post hoc analysis evaluated mean change from baseline to Week 16 in ACR components (tender joint count, swollen joint count, Physician's Global Assessment of PsA, Patients' Global Assessment of disease activity, Patients' Global Assessment of pain, and high-sensitivity CRP [hCRP]). Health Assessment Questionnaire-Disability Index (HAQ-DI) score through Week 16 and HAQ-DI response at Week 16 were predefined endpoints.

Results: Patients treated with deucravacitinib 6 mg and 12 mg QD were numerically more likely to achieve ACR20 response at Week 16 versus PBO regardless of TNFi experience (TNFi-naïve: 55.2% and 62.1% vs 32.7%; TNFi-experienced: 41.7% and 66.7% vs 27.3%, respectively) or body weight (<90 kg: 54.1% and 58.3% vs 37.5%; ≥90 kg: 51.5% and 67.7% vs 26.5%, respectively), although some groups were small. Improvements for deucravacitinib 6 mg and 12 mg QD versus PBO were observed in all ACR components, with apparent separation occurring as early as Week 4 on, for example, HAQ-DI (mean change from baseline, -0.2 and -0.2 vs -0.1, respectively) and hCRP (mean change from baseline, -7.4 and -5.2 vs 0.3, respectively) and maintained through Week 16.

Conclusion: Analyses confirmed the efficacy of deucravacitinib versus PBO across TNFi and body weight subgroups. With deucravacitinib treatment, improvements were displayed in all ACR components.

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Clinical utility of the 31-gene expression profile test on the management of cutaneous melanoma by nurse practitioners and physician assistants

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Introduction: The 31-gene expression profile (31-GEP) test for cutaneous melanoma (CM) assesses gene expression measurements from formalin-fixed paraffin-embedded primary tumor tissue to predict the tumor recurrence or metastasis risk. Risk predictions by the 31-GEP classify patients as having low (Class 1A), increased (Class 1B/2A), or high (Class 2B) biological risk. The focus of this study was to understand the perception and clinical application of the 31-GEP test specifically by nurse practitioners and physician assistants (NP/PAs).

Methods: A custom 20-question survey was made available to attendees of the Fall Clinical Dermatology 2020 conference and the 2020 Fall Clinical Dermatology Conference for PAs & NPs. The survey was designed to assess the attitudes of NP/PAs towards prognostic testing of CM, and specifically, about the 31-GEP test. Participation was voluntary and not associated with additional data presentation, and respondents that completed the survey were given monetary compensation. The data presented here are for participants that self-identified as NP/PAs (n=266/711 participants).

Results: The majority of participants (94%) indicated practice within the private sector, with 49% practicing for >10 years. Half of all respondents were users of the 31-GEP, having ordered the test at least once within the previous year. Interestingly, a trend indicated that more experienced practitioners (>10 years in practice) were more likely to be users of the test ($X^2 = 3.38$, $P = .07$). Approximately half of the participants were recent users of the 31-GEP test. In addition, 89% of NP/PAs reported their belief that comprehensive prognostic information improves patient care, with 97% of 31-GEP users indicating they would recommend additional prognostic testing (such as GEP) to close friends or family to aid in decision making compared to 58% of non-users ($X^2 = 58.19$, $P < .001$). Factors that increased a practitioner's likelihood of ordering the 31-GEP included increased Breslow thickness (89%), ulceration (61%), and mitotic rate >2/mm^2 (53%). For patients with thin (T1) tumors, 62% of all participants responded that a high-risk 31-GEP Class 2B result would motivate them to increase disease management intensity, which increased to 82% among recent test users ($X^2 = 43.33$, $P < .001$ vs. 43% of non-users). Although most patients with T1a tumors are likely to receive a low-risk 31-GEP result (89.3%), 74% percent reported value in the Class 1A result in relieving the uncertainty for their patients, and 55% valued the increased confidence in treatment plans provided by a biologically confirmed low-risk result. Finally, of those who use the 31-GEP test, 99% reported that they are very likely or somewhat likely to recommend the 31-GEP test to a colleague.

Conclusion: NP/PAs are actively using the 31-GEP in dermatology practice to improve prognostic accuracy and increase confidence in their treatment plans. Critically, an overwhelming majority of NP/PAs that use the 31-GEP test would recommend its use to colleagues.

Real-World Clinical Usage Data Demonstrates Appropriate Utilization of the Prognostic 40-Gene Expression Profile (40-GEP) Test for Cutaneous Squamous Cell Carcinoma (cSCC) with One or More Risk Factors

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Introduction: Although the metastatic rate for cSCC is low, the overall incidence is high, resulting in an annual death rate estimated to surpass that of melanoma. Patient risk for poor outcomes guides management decisions, thus accurate risk assessment is of utmost importance. Currently, a universal method of risk assessment has not been accepted for cSCC; histopathologic methods options include weighting of risk factors by individual physician judgement or the use of formalized staging systems (e.g. AJCC and Brigham and Women's Hospital (BWH) staging). The prognostic 40-GEP test was developed and validated to accurately classify risk for regional or distant metastasis as low (Class 1), moderate (Class 2A), or high (Class 2B) in patients with primary cSCC and one or more high-risk factors. The purpose of this study was to demonstrate independent prognostic value with existing risk assessment methods and report on the early clinical usage of the 40-GEP test.

Methods: Analysis of an expanded archival cohort of high-risk cSCC cases (n=420) was performd within a multi-institutional, IRB-approved study. Formalin-fixed paraffin-embedded primary cSCC tissue with verified clinicopathologic information, centralized pathology review, and outcomes data were assayed under clinical testing conditions in a CAP-accredited, CLIA-certified laboratory. Kaplan-Meier for metastasis-free survival (MFS), Cox regression analysis, and accuracy statistics were generated. Clinical usage metrics of the 40-GEP test were reported.

Results: The 3-year MFS rate for the validation cohort was 85.5% which was then stratified by 40-GEP result. A statistically significant difference was observed in

MFS: Class 1 (93.9%, n=212); Class 2A (80.5%, n=185); and Class 2B (47.8%, n=23); $p<0.001$, log-rank. The 40-GEP improved positive predictive value for metastasis to 52% compared to traditional staging systems. Increased risk for cSCC-specific deaths (n=18) was also demonstrated within the Class 2A and Class 2B groups with hazard ratios of 4.2 ($p=0.02$) and 14.8 ($p<0.001$), respectively. The 40-GEP demonstrated independent prognostic value using multivariable analysis, when accounting for either individual risk factors or formalized staging. Lesions submitted for clinical testing had 1-2 (48%), 3-4 (34%) or 5+ (18%) risk factors. Clinical cases were evenly distributed between T1-T3 AJCC T-stage, and the greatest frequency of BWH T-stage submitted was T2a.

Conclusions: The 40-GEP test is validated to classify risk for metastasis in cSCC patients with one or more risk factors and provides prognostic information independent from known high risk factors or established staging systems. The intended use population aligns with the cases submitted for clinical testing. Incorporating 40-GEP test results in clinical assessments may contribute to risk-appropriate surveillance and treatment decisions.

Tapinarof Cream 1% Once Daily for Plaque Psoriasis: Interim Analysis of a Long-Term Extension Trial of a Novel Therapeutic Aryl Hydrocarbon Receptor Modulating Agent

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Introduction: Tapinarof cream 1% once daily (QD) demonstrated significant efficacy versus vehicle and was well-tolerated in adults with mild to severe plaque psoriasis in two identical 12-week pivotal phase 3 trials (PSOARING 1 & 2). Furthermore, a 12-week phase 2b study showed efficacy maintenance after treatment discontinuation, warranting investigation of potential remittive effect. We present the interim report (November 2020) of PSOARING 3, a long-term, open-label, multicenter extension trial assessing safety, efficacy, durability of response, and duration of remittive effect of tapinarof cream 1% QD in adults with plaque psoriasis.

Methods: Eligible patients completing PSOARING 1 or 2 could enroll in PSOARING 3 for 40-weeks open-label treatment followed by 4-weeks follow-up, thus receiving up to 52 weeks of treatment. Patients entering with Physician Global Assessment (PGA) score ≥1 received tapinarof 1% QD until complete disease clearance (PGA=0). Patients entering with, or achieving, PGA=0 discontinued treatment and were monitored for duration of remittive effect: off-therapy maintenance of PGA=0 or 1 (clear or almost clear). Patients with disease worsening (PGA≥2) were re-treated with tapinarof until PGA=0. Patients were followed for durability of response on-therapy (no tachyphylaxis). Safety assessments included adverse events (AE) and patient- and investigator-rated local tolerability. Efficacy endpoints included median time from PGA=0 to first worsening, and proportion of patients with PGA=0 or 1 after treatment.

Results: Analysis included all enrolled patients (n=763), regardless of length of participation in PSOARING 3. AEs were similar to pivotal studies: most localized to application site, mild to moderate, and resulted in low discontinuations (5.8%) with no new safety signals, regardless of treatment duration. Most common AEs were folliculitis, contact dermatitis, and upper respiratory tract infection. Incidence and severity of folliculitis and contact dermatitis remained stable with long-term use and led to low study discontinuations (1.2% and 1.4%, respectively). Complete disease clearance (PGA=0) was achieved by 39.2% of patients (n=299). For patients entering with PGA=0 (n=78), median duration of remittive effect was 115 days. Response measures continued to improve beyond the 12-week pivotals: 57.3% of patients entering with PGA≥2 achieved PGA=0 or 1 at least once during PSOARING 3. Durability of response (no tachyphylaxis) was demonstrated for up to 52 weeks of treatment, with no decline over time.

Conclusion: Tapinarof cream 1% QD was well-tolerated with consistent long-term safety. The high rate of complete disease clearance, ~4-month remittive effect off-therapy, and no tachyphylaxis are key attributes differentiating tapinarof from other topical psoriasis therapies.

Tapinarof Cream 1% QD for the Treatment of Plaque Psoriasis: Efficacy and Safety in Two Pivotal Phase 3 Trials

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Introduction: Tapinarof is a novel therapeutic aryl

hydrocarbon receptor modulating agent (TAMA) in development for the treatment of psoriasis and atopic dermatitis. Here we present the efficacy and safety of tapinarof cream 1% QD in patients with mild to severe plaque psoriasis in two identical, randomized, double-blind, vehicle-controlled trials.

Methods: Adults with baseline Physician Global Assessment (PGA) score ≥2 and body surface area (BSA) involvement ≥3–≤20% were randomized 2:1 to tapinarof cream 1% or vehicle QD for 12 weeks. Primary efficacy endpoint was PGA response, defined as proportion of patients with PGA score of clear (0) or almost clear (1) and ≥2-grade improvement from baseline to Week 12; key secondary efficacy endpoint was ≥75% improvement in Psoriasis Area and Severity Index (PASI75) from baseline to Week 12. We report pivotal Phase 3 results for tapinarof cream 1% once daily (QD) in the treatment of plaque psoriasis.

Results: 510 and 515 patients were randomized in PSOARING 1 and PSOARING 2; overall at baseline, 79.2% and 83.9% of patients had PGA of 3; mean PASI was 8.9 and 9.1; mean BSA was 7.9% and 7.6%, respectively. At Week 12, both efficacy endpoints were met with high statistical significance (all $P<0.0001$): PGA response rates in the tapinarof 1% QD groups versus vehicle were 35.4% vs 6.0% and 40.2% vs 6.3%; and PASI75 rates in the tapinarof 1% QD groups versus vehicle were 36.1% vs 10.2% and 47.6% vs 6.9%. Most adverse events (AEs) were mild or moderate, consistent with previous studies, and did not lead to study discontinuation. Most common AEs (≥5% in any group) were folliculitis, nasopharyngitis, and contact dermatitis.

Conclusion: Tapinarof cream 1% QD demonstrated highly statistically significant and clinically meaningful efficacy compared with vehicle for both primary and secondary efficacy endpoints and was well-tolerated. Tapinarof cream has the potential to provide physicians and patients with a novel non-steroidal topical treatment option that is effective and well-tolerated.

Calcipotriene and betamethasone dipropionate cream demonstrates clinically meaningful improvement of itch associated to psoriasis

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Introduction: Calcipotriene and betamethasone dipropionate (0.005% / 0.064% w/w, CAL/BDP) cream is a novel FDA-approved topical treatment of plaque psoriasis under the brand name Wynzora® Cream. CAL/BDP cream is based on PAD™ Technology, which in a single product enables a combination of efficacy, safety and patient preference meeting the highlighted recommendations in the guideline for topical treatment of psoriasis issued by AAD and National Psoriasis Foundation. Data from a pivotal phase 3 trial is presented demonstrating substantial and clinically meaningful improvement of itch in psoriasis patients.

Methods: Itch was evaluated on an 11-point peak pruritus numeric rating scale (NRS). Itch reduction was evaluated by the absolute change in peak pruritus NRS score from baseline and by a responder analysis defining itch treatment success as at least 4 points improvement in peak pruritus NRS score from baseline. Patients were evaluated in a phase 3, randomized, multicenter, investigator-blind, parallel-group trial comparing CAL/BDP cream to vehicle and CAL/BDP topical suspension (TS) (sourced as Taclonex® Topical Suspension) in adult patients with plaque psoriasis. The trial enrolled 796 patients at 55 clinical sites across the United States of which 626 patients had a peak pruritus NRS score of at least 4 at baseline. Patients applied study medication once daily for eight weeks.

Results: CAL/BDP cream demonstrated superior reduction of peak pruritus NRS score compared to vehicle at Week 4 (3.5 vs 1.1 points of improvement; $p<0.0001$). CAL/BDP cream also demonstrated significant reduction in peak pruritus NRS score at Weeks 1 and 8. Among subjects who had at least a peak pruritus NRS score of 4 at baseline, there was a higher proportion of patients that achieved a clinically relevant improvement of at least 4 points from baseline to Week 4 in the CAL/BDP cream group compared to vehicle (60.3% vs. 21.4%; $p<0.0001$). CAL/BDP cream further demonstrated a significantly greater proportion of patients achieving at least 4 points improvement in peak pruritus NRS score during the first week of treatment in comparison to CAL/BDP TS (44.0% vs 36.9%; $p<0.0241$), thereby underlining the rapid onset of action for CAL/BDP cream.

Conclusions: Itch is a key symptom of plaque psoriasis. CAL/BDP cream, a novel topical treatment of psoriasis, demonstrated a substantial improvement of the proportion of patients achieving a minimum 4-point improvement on the peak pruritus NRS score at Week 4. Reduction of itch is included in the prescribing information.

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MC2-01 cream has improved overall psoriasis treatment efficacy compared to calcipotriene plus betamethasone dipropionate topical suspension

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Introduction: MC2-01 cream is a novel topical treatment of psoriasis containing the active ingredients calcipotriene and betamethasone dipropionate (0.005% / 0.064% w/w, CAL/BDP). MC2-01 cream is based on PAD™ Technology and designed for high penetration of the actives combined with excellent cosmetic elegance. Data from a phase 3 trial is presented comparing overall

efficacy of MC2-01 cream to CAL/BDP topical suspension ("CAL/BDP TS") in adults with mild to moderate psoriasis.

Methods: The phase 3, randomized, multicenter, investigator-blind, parallel-group trial evaluated the efficacy and safety of MC2-01 cream compared to MC2-01 vehicle and CAL/BDP TS (sourced as Taclonex® Topical Suspension) in adult patients with psoriasis vulgaris on the body. The trial enrolled 796 patients at 55 clinical sites across the United States: MC2-01 cream (n=343), CAL/BDP TS (n=338), MC2-01 vehicle (n=115). Patients applied trial medication once daily for eight weeks. The primary objective was to show therapeutic non-inferiority of MC2-01 cream to CAL/BDP TS, as well as to characterize the safety profile of MC2-01 cream in subjects with psoriasis vulgaris. The primary efficacy endpoint was the proportion of subjects with treatment success at Week 8, defined as minimum two-point decrease from baseline in Physician Global Assessment (PGA) score.

Results: The phase 3 trial met its primary objective to demonstrate non-inferiority of MC2-01 cream to CAL/BDP TS on PGA treatment success at Week 8 (MC2-01 cream 40.1% vs. CAL/BDP TS 24.0% vs. MC2-01 vehicle 4.5%). The primary objective was also met for the secondary endpoint percentage reduction in mPASI from baseline to Week 8. Additional analysis of PGA treatment success showed that MC2-01 cream is superior to CAL/BDP TS at Week 4 ($p<0.0001$) and Week 8 ($p<0.0001$). Further analyses of percentage reduction in mPASI from baseline confirmed that MC2-01 cream has superiority to CAL/BDP TS throughout treatment from Week 1 (26.2% vs. 18.9%, $p<0.001$) to Week 8 (64.8% vs. 52.3%, $p<0.0001$). MC2-01 cream also provided reduction in itch compared to vehicle measured by the proportion of patients having minimum 4-points improvement on an 11-point numeric rating scale of itch severity (60.2% 4 vs. 21.4% at Week 4, $p<0.01$). The safety profile of MC2-01 cream was similar to that known for CAL/BDP products.

Conclusions: The phase 3 trial showed that MC2-01 cream is a substantial improvement in overall efficacy and onset of action for topical treatment of psoriasis compared to CAL/BDP TS. Enhanced patient satisfaction enabled by the MC2-01 cream PAD™ Technology may increase treatment compliance among patients, and positively impact real-life treatment outcomes even further. As such PAD™ Technology holds the promise of redefining topicals.

Oxymetazoline and Energy-Based Therapy in Patients with Rosacea: Evaluation of the Safety and Tolerability in an Open-Label, Interventional Study

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Objectives: The objectives of this study were to evaluate the safety, tolerability, and efficacy of oxymetazoline hydrochloride cream, 1% (oxymetazoline) when used as an adjunctive treatment with energy-based therapy for patients with moderate to severe facial erythema associated with rosacea.

Methods: In this Phase 4, multicenter, interventional, open-label study, eligible patients received one of four energy-based therapies (potassium titanyl phosphate laser, intense pulsed light therapy, pulsed-dye laser Vbeam Perfecta, or pulsed-dye laser Cynergy) on day 1 and day 29 and once-daily application of oxymetazoline on days 3 through 27 and days 31 through 56. Improvement from baseline in Clinician Erythema Assessment (CEA) score, patient satisfaction measures, incidence of treatment-emergent adverse events (TEAEs) and worsening from baseline on dermal tolerability assessments and the Clinician Telangiectasia Assessment (CTA) were assessed. Data were summarized using descriptive statistics.

Results: A total of 46 patients (mean age, 51.1 years; 78.3% female) enrolled in the study. Similar numbers of patients received each of the energy-based therapies in addition to oxymetazoline. All patients demonstrated an improvement from baseline in CEA during the study with 39 of 43 evaluable patients (90.7%) demonstrating an improvement 6 hours posttreatment on day 56. Most patients were satisfied or very satisfied with treatment at the end of the study. All TEAEs were mild or moderate in severity. Some patients experienced worsening in dermal tolerability assessment symptoms (range: 4–21 patients; 8.7% to 45.7%). Worsening in CEA and CTA were each reported by three patients (6.5%) at any time during the study.

Conclusions: Treatment with oxymetazoline as adjunctive therapy with energy-based therapy was safe, well-tolerated, and reduced facial erythema in patients with moderate to severe persistent facial erythema associated with rosacea.

Maximizing Remission in Rosacea with Once Daily Subantibiotic Dose Oral Doxycycline 40 mg Modified-release Capsules

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Introduction: Maximizing the duration of remission by providing effective rosacea treatment is an important goal for clinicians, due to recurrent cycles of exacerbation and remission over the lifetime of their patients.[1] Treatment combining topical metronidazole gel 1% and *subantibiotic* dose doxycycline (dosing to avoid antibiotic resistance, previously referred to as *subantimicrobial*), administered

as once-daily 40 mg modified-release (MR) capsules (30 mg of immediate-release and 10 mg delayed-release [via beads]), has been shown to produce a more rapid and greater reduction of papules and pustules compared with topical metronidazole monotherapy.[2-3] However, the long-term efficacy of subantibiotic dose doxycycline (SDD_{40}) in sustaining remission of rosacea has not been previously investigated.

Methods: This 2-part study evaluated the efficacy of SDD_{40} monotherapy in extending the duration of rosacea remission. Part 1 was a multicenter, open-label, 12-week study in which adults with moderate or severe inflammatory lesions (papules and pustules) of rosacea received SDD_{40} and topical metronidazole gel 1%. Part 2 was a multicenter, randomized, double-blind, placebo-controlled, 40-week study in which successfully treated subjects received once-daily SDD_{40} or placebo capsules. The primary objective was to assess relapse and efficacy during long-term use of SDD_{40} versus placebo. Relapse was defined as a return to baseline Investigator's Global Assessment (IGA) or lesion count, or any other necessary change in treatment.

Results: Part 1 enrolled 235 subjects. Sixty-five subjects in the SDD_{40} treatment group and 65 subjects in the placebo group met the definition of treatment success at week 12, and were included in the part 2 analysis. At the end of part 2, half as many subjects treated with SDD40 had relapsed compared to placebo (13.8% [n = 9] vs. 27.7% [n = 18], respectively; $P < .05$). Significant differences in the median change in inflammatory lesion counts were also observed ($P < .05$). Adverse events (AEs) were generally mild or moderate in severity, and most AEs were not treatment-related. Stinging/burning was improved in subjects treated with SDD40 in parts 1 and 2.

Conclusion: After initial use of once daily treatment for 12 weeks, continued use of SDD^{40} significantly reduced the relapse rate and inflammatory lesion counts in subjects with moderate-to-severe rosacea at baseline.

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One Dose Fits All: Once Daily Subantibiotic Dose Oral Doxycycline 40 mg Modified-release Capsules Effective in Different BMIs and Across Severities of Papulopustular Rosacea

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Introduction: Rosacea is associated with multiple comorbidities (such as cardiovascular and gastrointestinal [GI] diseases) in a severity-dependent manner,[1] and an increased risk observed with obesity as shown by body mass index [BMI] in a dose-dependent manner.[2]

Subantibiotic dose (previously called *subantimicrobial*) oral doxycycline (40 mg modified release capsules [30 mg immediate-release, 10 mg delayed-release beads], or SDD_{40}) is the only FDA-approved oral therapy for inflammatory lesions (papules and pustules) of rosacea. In the interest of avoiding antibacterial resistance and improving tolerability, clinicians can prescribe antibiotics based on evidence supporting similar efficacy of doxycycline at lower doses compared to higher doses.[3] However, choosing the optimal dose and avoiding antibiotic resistance may seem challenging for patients affected by different severities or with co-morbidities.

To explore whether the patient's lesion severity or weight impacts the efficacy of SDD_{40}, the efficacy and safety of SDD_{40} in treating rosacea were evaluated.

Methods: A meta-analysis of two 16-week phase 3 multicenter, randomized, double-blind, placebo-controlled, parallel-group pivotal studies (n=142) was performed. For each study, percent change from baseline in inflammatory lesions was calculated, and weights were categorized into underweight (i.e. BMI <18.5), normal (BMI: 18.5-24.9), overweight (BMI: 25.0-29.9), and obese (BMI ≥30.0). Linear models (using analysis of variance [ANOVA] and the correlation coefficient) assessed how baseline lesion counts and weight affected the percent change from baseline.

Results: The efficacy of SDD_{40} against inflammatory lesions was similar regardless of the number of baseline lesions and weight. The correlation coefficient (0.1846) from the ANOVA test remained below 0.75, indicating that the relationship, if any, between weight, baseline lesions, and percent change from baseline in inflammatory lesions was weak. SDD^{40} showed a good safety profile, with no vaginal candidiasis or phototoxicity. Most AEs were mild or moderate, and no serious AE was related to the study drug.

Conclusion: Results of this meta-analysis support SDD^{40} as an optimal treatment regardless of the patient's weight or lesion severity, without the need for weight-based dosing.

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The Burden of Combined Facial and Truncal Acne

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Introduction: Facial acne vulgaris (FA) associated quality of life (QoL) burden is known to be high, with increased risk of depression and suicidal thoughts. However, there is little information on the combined burden of facial and truncal acne (TA), even though nearly half of acne patients have truncal involvement. In this study, we sought to better-understand the burden of combined moderate to severe FA+TA.

Material and Methods: Qualitative research via 60-minute in-depth-interview (IDI), 6 countries, 30 patients (17 women, 13 men) aged 13-40 (median 23). Patients had moderate to severe active FA+TA, and were currently using healthcare professional (HCP) prescribed medication. IDI moderation was based on a semi-directive guide. Treatment satisfaction, FA+TA impact on overall QoL and other predefined data were collected via IDI (5-point scales). Analysis was descriptive via a common analysis template at country and globally levels.

Results: The patient initiated TA discussion in ~50% of instances (not the HCP). For ~75%, treatment recommendations were similar for FA+TA. Respondents were slightly less satisfied with TA vs FA treatment (average score of 3.13 vs 3.40, 5-point scale [5 - *extremely satisfied*, 0 - *not at all satisfied*]) due to treatment application difficulty and non-adherence. Both FA+TA negatively affected QoL, but FA impact was significantly greater (average 3.80 vs 2.90; *P*<.001). FA impact was also greater vs TA on all QoL subdimensions except for the *type of style, clothing, haircut* (3.10 average score vs 2.33) as patients expressed the need to cover areas affected by TA. However, even if respondents felt relief in covering/hiding their TA, TA continued to weigh on their *self-esteem* (average score 3.17) and on their intimate lives. *Hygiene habits* was ranked most impacted for both FA+TA; *self-esteem* ranked 2nd for TA while for FA it was ranked 3rd, closely after *social life*. Patients considered TA an *"additional nuisance"* and *"embarrassment"* (verbatim). An additional and specific impact of TA is physical pain, spontaneously mentioned by ~30% of the study participants (6 women and 4 men).

Discussion: TA is often disregarded by HCPs and consequently neglected by the patients themselves. Patients with combined FA+TA tend to diminish the negative impact of TA as it can be hidden by clothing. This study showed that, when both present, FA+TA highly impact QoL, and the combined impact is higher than with FA alone. Raising awareness of TA could improve clinical management and the QoL of affected patients.

Itch-Free State in Patients With Atopic Dermatitis Treated With Ruxolitinib Cream

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Atopic dermatitis (AD) is a highly pruritic, inflammatory skin disease. Inadequate control of AD is associated with greater itch interference with daily living. Janus kinases (JAKs) play an important role in the pathogenesis of AD and the development of itch by mediating proinflammatory cytokines in skin and sensory neurons. Ruxolitinib cream is a topical selective inhibitor of JAK1 and JAK2 in development for the treatment of AD. In two phase 3 studies (TRuE-AD1 [NCT03745638]; TRuE-AD2 [NCT03745651]), 1249 patients (≥12 years) with AD for ≥2 years, an Investigator's Global Assessment (IGA) score of 2 or 3, and 3%–20% affected body surface area were randomized (2:2:1) to twice-daily 0.75% ruxolitinib cream, 1.5% ruxolitinib cream, or vehicle cream for 8 weeks of double-blinded treatment. In this pooled analysis, effects of ruxolitinib cream on itch were assessed by the proportion of patients achieving an itch Numerical Rating Scale score of 0 or 1 (NRS 0/1) and no days of itch per Item 1 (frequency of itch) of the Patient-Oriented Eczema Measure (POEM). At Week 8, more patients who applied ruxolitinib cream (0.75%/1.5%) vs vehicle achieved NRS 0/1 (45.5%/51.5% vs 23.1%; *P*<0.0001); median time to NRS 0/1 was significantly shorter with ruxolitinib cream vs vehicle (12.0/8.0 days vs 51.0 days; *P*<0.0001). More patients achieved no days of itch per POEM with ruxolitinib cream (28.3%/32.9%) vs vehicle (9.0%; both *P*<0.0001). As assessed by NRS 0/1 or POEM, more patients achieved itch-free status at Week 8 with ruxolitinib cream vs vehicle (47.7%/52.0% vs 23.4%; both *P*<0.0001) regardless of baseline itch score (baseline itch NRS <6: 57.4%/58.1% vs 27.5%, *P*<0.0001; baseline itch NRS ≥6: 34.2%/41.3% vs 17.7%, *P*<0.01). Ruxolitinib cream was well tolerated with an adverse event (AE) profile similar to vehicle; no serious AEs were related to ruxolitinib cream. In summary, a significant number of patients with AD treated with ruxolitinib cream achieved and sustained an itch-free state and had a substantially shorter median time to NRS 0/1 vs vehicle.

Author Disclosures:
AB has served as a scientific advisor and/or clinical study investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte

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Long-Term Safety and Disease Control of Ruxolitinib Cream Among Adolescents With Atopic Dermatitis: Results From Two Phase 3 Studies

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Introduction: Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease often beginning in childhood and persisting into adolescence and adulthood. Ruxolitinib cream is a Janus kinase (JAK) 1/JAK2 inhibitor in development for the treatment of AD. In two phase 3 studies (TRuE-AD1 [NCT03745638]; TRuE-AD2 [NCT03745651]), 1249 patients (≥12 years old with AD for ≥2 years, Investigator's Global Assessment [IGA] score of 2/3, and 3%–20% affected body surface area [BSA]) were randomized (2:2:1) to twice-daily 0.75% ruxolitinib cream, 1.5% ruxolitinib cream, or vehicle cream for an 8-week double-blind vehicle-controlled period (continuous treatment) followed by a double-blind long-term safety (LTS) period (patients assessed every 4 weeks) up to Week 52. Patients initially randomized to ruxolitinib cream remained on their regimen during the LTS; patients initially on vehicle were rerandomized (1:1) to either ruxolitinib cream strength. During the LTS period, patients treated skin areas with active AD only and stopped treatment 3 days after clearance of lesions. Patients restarted AD treatment at first sign of recurrence. In this analysis, long-term disease control and safety of 0.75%/1.5% ruxolitinib cream for the full 52-week study period in adolescents (aged 12–17 years) with AD in TRuE-AD1 (assessed for disease control, n=46/n=41) and TRuE-AD2 (n=43/n=36) were evaluated. Most patients who applied 0.75%/1.5% ruxolitinib cream maintained no or minimal lesions (IGA 0/1) during Weeks 12–52 in TRuE-AD1 (range, 59.0%–78.8%/57.1%–78.4%) and TRuE-AD2 (range, 55.9%–73.5%/50.0%–74.1%). Mean BSA affected by AD during the LTS period was generally <3%, attesting to a mild/limited extent of disease. In a pooled safety analysis among adolescents, 64 (59.3%) and 43 (46.7%) patients on 0.75% (n=108) or 1.5% (n=92) ruxolitinib cream, respectively, experienced treatment-emergent adverse events (TEAEs) over the 52-week period; none were serious. The frequency of application site reactions was low. There were 7 (6.5%) and 3 (3.3%) patients on 0.75% or 1.5% ruxolitinib cream, respectively, with treatment-related adverse events over the 52-week period. TEAEs resulting in discontinuation were noted in 3 patients (2.8%) in the 0.75% ruxolitinib cream group and no patients in the 1.5% ruxolitinib cream group. In summary, ruxolitinib cream was well tolerated and not associated with any safety concerns during long-term therapy. Additionally, intermittent treatment with ruxolitinib cream provided adequate long-term disease control in adolescents with AD.

Author Disclosures:

LFE has served as an investigator, consultant, speaker, or data safety monitoring board member for AbbVie, Almirall, Arcutis, Asana, Dermavant, Eli Lilly, Forte Biosciences, Galderma, Ichnos/Glenmark, Incyte Corporation, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Otsuka, Pfizer, Regeneron, and Sanofi Genzyme. ELS is an investigator for AbbVie, Eli Lilly, Galderma, Kyowa Hakko Kirin, LEO Pharma, Merck, Pfizer, and Regeneron and is a consultant with honorarium for AbbVie, Eli Lilly, Forte Bio, Galderma, Incyte Corporation, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant. KP has received honoraria or clinical research grants as a consultant, speaker, scientific officer, advisory board member, and/or steering committee member for AbbVie, Akros, Amgen, Anacor, Arcutis, Astellas, Bausch Health/Valeant, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite, Celgene, Coherus, Dermira, Dow Pharmaceuticals, Eli Lilly, Galderma, Gilead, GlaxoSmithKline, Incyte Corporation, InflaRx, Janssen, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, Merck (MSD), Merck Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi- Aventis/Genzyme, Sun Pharmaceuticals, Takeda, and UCB. JCS has served as an advisor for AbbVie, LEO Pharma, Novartis, Pierre Fabre, Menlo Therapeutics, and Trevi; has received speaker honoraria from AbbVie, Eli Lilly, Janssen-Cilag, LEO Pharma, Novartis, Sanofi Genzyme, and Sun Pharma; and has received clinical trial funding from AbbVie, Almirall, Amgen, Galapagos, Holm, Incyte Corporation, InflaRX, Janssen-Cilag, Menlo Therapeutics, Merck, Novartis, Pfizer, Regeneron, Trevi, and UCB. LK has served as an investigator, consultant, or speaker for AbbVie, Amgen, Anaptys, Arcutis, Dermavant, Eli Lilly, Glenmark, Incyte Corporation, Kamedis, LEO Pharma, L'Oreal, Menlo, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Taro. DT has served as an investigator for AbbVie, Amgen, Arcutis, Astellas, Astion, Avillion, Boehringer Ingelheim, Celgene, Dermira, DS BioPharma, Dow Pharmaceuticals, Eli Lilly, F. Hoffmann-La Roche Ltd, Galderma, GlaxoSmithKline, Incyte Corporation, Isotechnika, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, and UCB Biopharma. SBF has received honoraria, clinical research grants, or fees as a consultant, speaker, advisory board member, and/or investigator for AbbVie, Aclaris Therapeutics, Asana BioSciences, AstraZeneca, Athenex, Celgene Corporation, Cutanea Life Sciences, Eli Lilly, Incyte Corporation, Innovaderm Research, Novartis, Pfizer, Promius Pharma, Regeneron, UCB, Valeant Pharmaceuticals North America, and XBiotech. MEK was an employee and shareholder of Incyte Corporation at the time this study was conducted. MEV and HR are employees and shareholders of Incyte Corporation. ASP has served as an investigator, speaker, or data safety monitoring board member for AbbVie, Abeona, Almirall, Anaptysbio, Asana, Boehringer Ingelheim, Bridgebio, Dermavant, Dermira, Eli Lilly, Exicure, Forte, Galderma, Incyte Corporation, InMed, Janssen, Lenus, LEO Pharma, Lifemax, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sol Gel, and UCB.

Long-Term Safety and Disease Control With Ruxolitinib Cream in Atopic Dermatitis: Results From Two Phase 3 Studies

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Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease. Ruxolitinib cream is a Janus kinase (JAK) 1/JAK2 inhibitor in development for treating AD. In two phase 3 studies (TRuE-AD1 [NCT03745638];TRuE-AD2 [NCT03745651]), 1249 patients (≥12 years old with AD for ≥2 years, Investigator's Global Assessment (IGA) score of 2/3, 3%–20% affected body surface area [BSA]) were randomized (2:2:1) to twice-daily 0.75% ruxolitinib cream, 1.5% ruxolitinib cream, or vehicle cream for an 8-week, double- blind, vehicle-controlled period (continuous treatment) followed by a double-blind long- term safety (LTS) period (assessments every 4 weeks) up to Week 52. Patients initially randomized to ruxolitinib cream remained on their regimen during the LTS period; patients initially on vehicle were rerandomized (1:1) to either ruxolitinib cream strength. During the LTS period, patients treated areas with active AD only and stopped treatment 3 days after clearance of lesions. Patients restarted treatment upon recurrence. In this analysis, long-term safety and disease control of 0.75%/1.5% ruxolitinib cream in patients who continued their original ruxolitinib cream strength regimen during the LTS period in TRuE-AD1 (n=222/225) and TRuE-AD2 (n=204/221) were evaluated. Most patients who applied 0.75%/1.5% ruxolitinib cream maintained no or minimal lesions (IGA score of 0/1) during Weeks 12–52 in TRuE-AD1 (range, 62.4%–76.9%/66.5%–77.3%) and TRuE-AD2 (59.6%–76.7%/72.0%–80.1%). Mean total affected BSA was <3% throughout the LTS period with 1.5% ruxolitinib cream in TRuE-AD1 (range of mean values, 1.5%–2.5%) and TRuE-AD2 (1.4%–2.1%) and in the 0.75% ruxolitinib cream arm during most of the LTS period (TRuE-AD1, 1.5%–3.2%; TRuE-AD2, 2.2%– 3.3%). In a pooled safety analysis, 256 (60.1%) and 240 (53.8%) patients who applied 0.75% (n=426) and 1.5% (n=446) ruxolitinib cream, respectively, reported treatment-emergent adverse events (AEs) over the 44-week LTS period. Frequency of application site reactions remained low. There were 20 (4.7%) and 13 (2.9%) patients on 0.75% and 1.5% ruxolitinib cream, respectively, with treatment-related AEs; none were serious. Treatment-emergent AEs resulted in discontinuation in 9 patients (2.1%) with 0.75% ruxolitinib cream and no patients with 1.5% ruxolitinib cream. In summary, approximately 70% of patients maintained no or minimal lesions (IGA score of 0/1), and the extent of AD lesions (percentage affected BSA)

remained low during the 44-week LTS period, indicating that patients achieved long-term disease control with ruxolitinib cream. Ruxolitinib cream was well tolerated in the long-term setting, with no serious treatment-related AEs.

Author Disclosures:
KP has received honoraria or clinical research grants as a consultant, speaker, scientific officer, advisory board member, and/or steering committee member for AbbVie, Akros, Amgen, Anacor, Arcutis, Astellas, Bausch Health/Valeant, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite, Celgene, Coherus, Dermira, Dow Pharmaceuticals, Eli Lilly, Galderma, Gilead, GlaxoSmithKline, Incyte Corporation, InflaRx, Janssen, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, Merck (MSD), Merck Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharmaceuticals, Takeda, and UCB. JCS has served as an advisor for AbbVie, LEO Pharma, Novartis, Pierre Fabre, Menlo Therapeutics, and Trevi; has received speaker honoraria from AbbVie, Eli Lilly, Janssen-Cilag, LEO Pharma, Novartis, Sanofi Genzyme, and Sun Pharma; and has received clinical trial funding from AbbVie, Almirall, Amgen, Galapagos, Holm, Incyte Corporation, InflaRX, Janssen-Cilag, Menlo Therapeutics, Merck, Novartis, Pfizer, Regeneron, Trevi, and UCB. LK has served as an investigator, consultant, or speaker for AbbVie, Amgen, Anaptys, Arcutis, Dermavant, Eli Lilly, Glenmark, Incyte Corporation, Kamedis, LEO Pharma, L'Oreal, Menlo, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Taro. DT has served as an investigator for AbbVie, Amgen, Arcutis, Astellas, Astion, Avillion, Boehringer Ingelheim, Celgene, Dermira, DS BioPharma, Dow Pharmaceuticals, Eli Lilly, F. Hoffmann-La Roche Ltd, Galderma, GlaxoSmithKline, Incyte Corporation, Isotechnika, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, and UCB Biopharma. LFE has served as an investigator, consultant, speaker, or data safety monitoring board member for AbbVie, Almirall, Arcutis, Asana, Dermavant, Eli Lilly, Forte Biosciences, Galderma, Ichnos/Glenmark, Incyte Corporation, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Otsuka, Pfizer, Regeneron, and Sanofi Genzyme. SBF has received honoraria, clinical research grants, or fees as a consultant, speaker, advisory board member, and/or investigator for AbbVie, Aclaris Therapeutics, Asana BioSciences, AstraZeneca, Athenex, Celgene Corporation, Cutanea Life Sciences, Eli Lilly, Incyte Corporation, Innovaderm Research, Novartis, Pfizer, Promius Pharma, Regeneron, UCB, Valeant Pharmaceuticals North America, and XBiotech. MEK was an employee and shareholder of Incyte Corporation at the time this study was conducted. MEV and KS are employees and shareholders of Incyte Corporation. ELS is an investigator for AbbVie, Eli Lilly, Galderma, Kyowa Hakko Kirin, LEO Pharma, Merck, Pfizer, and Regeneron and is a consultant with honorarium for AbbVie, Eli Lilly, Forte Bio, Galderma, Incyte Corporation, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant.

Long-term improvements observed in tralokinumab-treated patients with moderate-to-severe atopic dermatitis: an ECZTEND interim analysis

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Introduction: Additional long-term treatment options are needed for patients with moderate-to-severe atopic dermatitis (AD). Tralokinumab is a fully human monoclonal antibody that specifically targets interleukin-13, a key driver of AD signs and symptoms.[1,2]

Methods: The efficacy and safety of tralokinumab for up to 52 weeks in adult patients with AD have been published previously.[3,4] An ongoing, 142-week, open-label extension trial (ECZTEND; NCT03587805) is investigating the long-term safety and efficacy of tralokinumab 300 mg q2w in patients who previously participated in tralokinumab AD trials. We present interim efficacy results based on Investigator's Global Assessment (IGA) and Eczema Area Severity index (EASI) scores.

Results: Overall, 1174 patients were included in ECZTEND at data cut-off (April 2020). Outcomes were analyzed as observed at Week 56, and included all patients enrolled 60 weeks prior to data cut-off (N=612). Median time since last treatment dose in parent trials[3-5] to first treatment dose in ECZTEND was 36 days. Median age was 38 years, 57% were male, and median duration of AD was 27 years at baseline for all patients. At parent-trial baseline, ECZTEND baseline, and Week 56, median (IQR) EASI scores were 26.9 (19.7-37.3), 4.8 (2.0-12.6), and 1.8 (0.4-5.6), respectively. At Week 56, IGA and EASI response rates were 49.7% (IGA 0/1), 95.1% (EASI-50), 82.8% (EASI-75), 61.0% (EASI-90), and 79.7% (EASI ≤7). Sensitivity analyses were consistent with efficacy of all observed patients. Safety data remained consistent with that in the parent trials.

Conclusion: These data support that tralokinumab can lead to long-term improvements and is well-tolerated in patients with moderate-to-severe AD.

Funding Source. The ECZTEND study is sponsored by LEO Pharma A/S, Ballerup, Denmark.

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Tralokinumab prevents flares in moderate-to-severe atopic dermatitis: post hoc analysis of a randomized phase 3 clinical trial (ECZTRA 3)

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Introduction: Atopic dermatitis (AD) is a chronic, inflammatory skin disease characterized by periods of acute symptomatic worsening (flares). Tralokinumab is a fully human, high-affinity, monoclonal antibody that specifically neutralizes the interleukin (IL)-13 cytokine, a key driver of cutaneous barrier dysfunction, inflammation, and dysbiosis in AD. Flare-prevention is a primary goal for long-term AD control. We assessed the impact of tralokinumab treatment on flare prevention in adults with moderate to-severe AD.

Methods: ECZTRA 3 was a randomized, double-blind, placebo-controlled phase 3 trial in adults with moderate-to-severe AD (NCT03363854).[1] AD flares, defined as worsening of disease that required escalation/intensification of AD treatment including initiation or intensification of the supplied TCS ('per protocol flare'), were measured throughout the trial (32 weeks). We present a post-hoc analyses of flare occurrence, as defined by treatment intensification to either high-potency TCS, oral corticosteroids, or other systemic treatments ('rescue flare').

Results: Treatment groups were well-balanced with respect to baseline AD severity. Overall, 7 patients (2.8%) reported a 'rescue flare' in the tralokinumab+TCS group, compared with 13 (10%) in the placebo+TCS group during the first 16 weeks, corresponding to a 74% risk reduction with tralokinumab (P=0.004). Similarly, 6 patients (2.4%) reported an 'AE flare' in the tralokinumab+TCS group vs 14 (11%) with placebo+TCS during the first 16 weeks, corresponding to an 80% risk reduction with tralokinumab (P=0.001). The risk of a 'rescue flare' or 'AE flare' (which ever occurred first) was 77% lower with tralokinumab (P<0.001). The proportion of patients with a 'per protocol flare' during the initial 16-week treatment period was numerically lower in the tralokinumab+TCS group (28%, 70/252) compared with the placebo+TCS group (34%, 43/126). Among patients who received tralokinumab+TCS during the 32-week treatment period, 65% (163/252) did not report a 'per protocol flare', and nearly all did not report a 'rescue flare' (96%, 241/252) or an 'AE flare' (94%, 236/252) during the 32 weeks. The cumulative amount of TCS used was approximately 30% lower in tralokinumab+TCS group compared with the placebo+TCS group, both in the overall population and among patients who reported a 'per protocol flare' between Week 0 and 16.

Conclusion: Tralokinumab treatment was associated with a reduced risk of AD flares when used in combination with TCS in adults with moderate-to-severe AD. Most patients who received tralokinumab+TCS during the entire 32-week remained flare-free.

Funding Source: The ECZTRA 3 trial was sponsored by LEO Pharma A/S, Ballerup, Denmark.

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Impact of Secukinumab on Clinical and Patient-Reported Outcomes in Biologic-Naive Patients With Psoriasis in a US Real-World Setting

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Background: In prior CorEvitas' Psoriasis Registry studies, patients with psoriasis (PsO) who initiated secukinumab exhibited clinically meaningful response in clinical and patient-reported outcomes (PRO) at 6, 12, and 18 months[1,2]; however, the majority of patients in these studies used multiple other biologics prior to secukinumab. The objective of this study was to describe patient characteristics and effectiveness among patients who initiated secukinumab, stratified by prior biologic exposure status.

Methods: This study included US patients with PsO who initiated secukinumab in CorEvitas' Psoriasis Registry at or after enrollment and had a subsequent 6- and/or 12-month follow-up visit at which they remained on secukinumab (4/2015-12/2020). Demographics, clinical characteristics, treatment history, disease activity (IGA, PASI, and BSA) and PRO measures (DLQI, EQ-5D-3L, EQ-VAS, patient global assessment, itch, skin pain, and WPAI) were evaluated at secukinumab initiation and follow-up. Analyses were stratified by biologic exposure status at therapy initiation (naive vs experienced) and were conducted separately for 3 cohorts of patients who had follow-up visits at 6 months,12 months, and both 6 and 12 months.

Results: Of 1518 patients who initiated secukinumab, 652 had a 6-month visit (192 [29.4%] biologic naive, 460 [70.6%] biologic experienced), 390 had a 12-month visit (102 [26.2%] naive, 288 [73.8%] experienced), and 326 had both 6- and 12-month visits (82 [25.2%] naive, 244 [74.8%] experienced). Among patients who remained on secukinumab at 12 months, mean age at

PsO diagnosis was 37.4 and 32.8 years for biologic-naive and biologic-experienced patients, respectively; 33.3% and 59.8% of biologic-naive and biologic-experienced patients, respectively, had comorbid psoriatic arthritis. Both biologic-naive and biologic-experienced patients demonstrated improvements from baseline in continuous disease activity outcomes and PRO measures at 6 months that were sustained through 12 months including IGA (change from baseline to 6/12 months; naive: −1.7/−1.9; experienced: −1.4/−1.6), PASI (−6.7/−6.9; −5.2/−5.1), EQ VAS (6.9/10.3; 6.5/7.0), and work impairment due to PsO (−9.6%/−9.5%; −8.1%/−8.4%). Patients also shifted to improved disease activity and PRO categories—eg, BSA ≥3% to <3% (6/12 months; naive: 73.4%/83.0%; experienced: 62.8%/67.8%), IGA moderate/severe to clear/almost clear (63.9%/69.7%; 50.3%/55.6%), and DLQI ≥6 to 0-5 (78.8%/83.6%; 68.8%/72.3%).

Conclusions: In this real-world study of patients with PsO, both biologic-experienced and biologic-naive patients who initiated and maintained treatment with secukinumab demonstrated improvements in disease activity and PROs at 6- and 12-month follow-up. These findings suggest that secukinumab is effective in patients who remain on treatment regardless of prior exposure to biologics and is a viable first-line biologic for PsO.

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Restricted Mean Survival Time (RMST) and Cure-Rate Modeling in Estimating Survival Benefit with Adjuvant Dabrafenib (D) Plus Trametinib (T) Treatment in Melanoma

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Background: Kaplan-Meier and Cox regression are used to determine relapse-free survival (RFS) and treatment effects, but do not account for nonproportional hazards and/or fraction of patients that may never have disease relapse. Therefore, in COMBI-AD, we evaluated treatment effects using RMST, which assesses survival AUC and cure-rate analysis.

Methods: COMBI-AD (NCT01682083) is a randomized phase III trial that compared 12 months of adjuvant D 150 mg BID + T 2 mg QD vs matched placebos (PBO) in patients with resected stage III mutant melanoma, stratified by *BRAF* V600E/K status and AJCC 7 disease stage. RMST truncated at 60 months and a mixed Weibull cure-rate model were used to estimate treatment effect and RFS rates.

Results: Median follow-up in the D+T and PBO arms was 60 and 58 months, respectively. At the data cutoff (Nov 8, 2019), RMST was 41.5 months (95% CI, 39.4-43.6 months) with D+T vs 28.7 months (95% CI, 26.3-31.2 months) with PBO, representing 12.8 month gain with D+T over 60 months. The overall cure rate was 51% (95% CI, 46%-56%) with D+T vs 35% (95% CI, 30%-40%) with PBO, demonstrating a 16% increase in patients who remain relapse free with D+T. RMST and cure rate were improved with D+T across AJCC 7 substages, with the greatest benefit observed in patients with stage IIIB or IIIC.

Conclusions: COMBI-AD RMST and cure-rate models demonstrate significant benefit with adjuvant D+T across all melanoma stage III substages and may assist oncologists with presenting adjuvant stage III options to their patients.

Disclosures: This submission is an encore abstract that was previously presented at ESMO 2020 (abstract 2614).

A Novel Lotion Formulation for Enhanced Drug Permeation and Patient Adherence in Psoriasis Treatment

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Introduction: Topical corticosteroids represent a cornerstone treatment of lesion and symptom resolution in psoriasis. Features of topical drug formulations can greatly influence treatment efficacy and patient adherence. Patient preference is greater for vehicle

formulations that are effective, quickly absorbed, lightweight, and less oily/sticky. A novel, low-irritancy, nongreasy lotion formulation that utilizes an oil-in-water emulsion (polymeric emulsion technology) poses unique advantages over traditional creams and ointments. Upon contact with the skin, the active drug and hydrating ingredients of the formulation are uniformly and rapidly delivered into the skin. Incorporating this technology, the safety and efficacy profile of fixed-combination halobetasol propionate (0.01%) and tazarotene (0.045%) lotion (HP/TAZ) in plaque psoriasis has been established. Herein, we compare the permeation efficacy of HP/TAZ with HP or TAZ cream alone and assess patient preferences for use of the novel, fixed-combination HP/TAZ in treatment of psoriasis.

Methods: Percutaneous permeation studies were used to compare in vitro dermal deposition of fixed-combination HP/TAZ with HP (0.05%) cream and TAZ (0.1%) cream individually. Patient preferences for several features of fixed-combination HP/TAZ were assessed via an 18-question survey administered to 15 respondents.

Results: Higher cutaneous permeation efficiency of active ingredients into dermal layers was demonstrated with HP/TAZ vs HP or TAZ cream alone. Additionally, layering TAZ cream onto HP cream decreased cutaneous permeation of TAZ. Among all questions asked regarding the formulation attributes of HP/TAZ, including degree of skin hydration; softness, smoothness, and nongreasiness of skin feel; lightweight moisturization; and rapidity of absorption into the skin, most participants (93% to 100%) responded positively (strongly agree or agree).

Conclusions: Formulation of HP/TAZ lotion resulted in higher permeation efficiency of active ingredients compared with application of HP or TAZ cream alone and is agreeable to nearly 100% of patients. The novel HP/TAZ lotion formulation may provide a more effective, patient-preferred, and long-term treatment option than cream formulations.

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Effects of Tazarotene 0.045% Lotion on Moderate-to-Severe Acne in Patients With Skin of Color

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**Bausch Health US, LLC is an affiliate of Bausch Health Companies Inc. Ortho Dermatologics is a division of Bausch Health US, LLC.*

Introduction: Acne vulgaris affects all skin types and ethnicities, but patients with skin of color (SOC) are more likely to experience hyperpigmentation. Topical retinoids are effective in reducing acne lesions and related hyperpigmentation, although local skin reactions may limit their use. Results from two identical phase 3 studies (NCT03168321, NCT03168334) showed that tazarotene 0.045% lotion was efficacious and safe in treating moderate-to-severe acne. Data from these two studies were pooled to evaluate its effects in patients with SOC.

Methods: Eligible participants—aged ≥9 years with an Evaluator's Global Severity Score (EGSS) score of 3 (moderate) or 4 (severe)—were randomized (1:1) to once-daily tazarotene 0.045% lotion or vehicle lotion for 12 weeks. Efficacy endpoints included changes from baseline in inflammatory/noninflammatory lesion counts and treatment success (≥2-grade reduction from baseline in EGSS and score of 0=clear or 1=almost clear). Hyperpigmentation (0=none to 3=severe) was also evaluated. Descriptive post hoc analyses were conducted in self-identified Black, Asian, and Hispanic/Latino participants; race (Black, Asian) and ethnicity (Hispanic/Latino) were not mutually exclusive categories.

Results: Among 799 tazarotene-treated participants in the overall pooled intent-to-treat population, 125 (15.6%) were Black, 168 (21.0%) were Hispanic, and 42 (5.3%) were Asian. At week 12, least-squares mean inflammatory lesion reductions in tazarotene-treated SOC subgroups (Black: -60.4%; Asian: -56.0%; Hispanic: -60.0%) were generally similar to the overall population (-57.9%). Reductions in noninflammatory lesions were also similar between the tazarotene-treated SOC subgroups (Black: -52.6%; Asian: -59.5%; Hispanic: -56.0%) and the overall population (-56.0%). Hyperpigmentation severity decreased from baseline to week 12 in all tazarotene-treated subgroups.

Conclusions: After 12 weeks of tazarotene 0.045% lotion treatment, acne improvements were generally found among Black, Asian, and Hispanic patients, and were similar to those in the overall population. Hyperpigmentation severity also decreased in SOC participants. Overall, tazarotene 0.045% lotion may be an effective and well-tolerated treatment option for acne and acne-related hyperpigmentation in patients with SOC.

Funding: Ortho Dermatologics

Efficacy and Safety of Brodalumab in Patients With Inadequate Response to Ustekinumab: Analysis of Two Phase 3 Psoriasis Studies

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**Bausch Health US, LLC is an affiliate of Bausch Health Companies Inc; Ortho Dermatologics is a division of Bausch Health US, LLC.*

Introduction: Brodalumab, a fully human anti–interleukin-17 receptor A monoclonal antibody, antagonizes inflammatory cytokines involved in psoriasis pathogenesis. This post hoc analysis of two phase 3 psoriasis studies (AMAGINE-2/-3) evaluated the efficacy and safety of brodalumab in patients initially randomized to ustekinumab (an anti–interleukin-12/-23 monoclonal antibody) who were rescued with brodalumab after an inadequate clinical response to ustekinumab.

Methods: After a 12-week induction phase during which patients were randomized 2:2:1:1 to brodalumab 210 mg every 2 weeks (Q2W), brodalumab 140 mg Q2W, ustekinumab (45 mg for patients ≤100 kg or 90 mg for patients >100 kg on day 1 and week 4), or placebo, patients received maintenance treatment as follows: brodalumab-treated patients were rerandomized to brodalumab 210 mg Q2W, 140 mg Q2W, 140 mg Q4W, or 140 mg Q8W; ustekinumab-treated patients continued to receive ustekinumab; and those receiving placebo switched to brodalumab 210 mg Q2W. At week 16, patients with inadequate response (single static physician's global assessment [sPGA] of ≥3 or persistent sPGA of 2 over ≥4 weeks) were eligible for rescue with brodalumab 210 mg Q2W. After week 16, patients on ustekinumab with an inadequate response remained on ustekinumab.

Results: A total of 590 patients were randomized to ustekinumab during the induction phase, of which 124 were rescued with brodalumab at week 16 because of an inadequate response. Before rescue (at week 12), psoriasis area and severity index 75%, 90%, and 100% response rates (PASI 75, 90, and 100) in patients randomized to ustekinumab who were eventually rescued with brodalumab were 24%, 5%, and 0%, respectively. After rescue with brodalumab 210 mg, PASI 75, 90, and 100 response rates in these patients increased to 73%, 58%, and 36%, respectively, at week 52. Similarly, the sPGA ≤1 response rate increased from 2.4% at week 12 to 60.5% at week 52. In ustekinumab-treated patients rescued with brodalumab, the rate of treatment-emergent adverse events through week 52 was 377.3 events per 100 patient-years and the rate of serious adverse events was 4.3 per 100 patient-years. No life-threatening or fatal adverse events were reported in these patients.

Conclusions: In patients with an inadequate response to ustekinumab, brodalumab may be a safe and effective alternative treatment.

Funding: This study was sponsored by Ortho Dermatologics (a division of Bausch Health US, LLC).

Encore: Data from this abstract were previously presented in full at the American Academy of Dermatology Annual Meeting; February 16-20, 2018; San Diego, CA; and Maui Derm for Dermatologists; January 25-29, 2020; Maui, HI.

Fixed-Combination Halobetasol Propionate and Tazarotene Lotion Reduces Signs and Symptoms of Psoriasis in Patients With Body Surface Area Involvement of 3% to 5%

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Introduction: Fixed-combination halobetasol propionate (0.01%) and tazarotene (0.045%) lotion (HP/TAZ) is approved for topical treatment of plaque psoriasis in adults.[1] Joint AAD-NPF guidelines recommend the combined use of TAZ with topical steroids for mild-to-moderate psoriasis.[2] Patients with body surface area (BSA) involvement of 3% to 5% and Dermatology Life Quality Index (DLQI) of <5 may be good candidates for combined topical therapy.

Methods: Two phase 3, multicenter, double-blind trials (ClinicalTrial.gov identifiers: NCT02462070, NCT02462122) enrolled 418 adults with BSA involvement of 3% to 12% and investigator's global assessment (IGA) of 3 (moderate) or 4 (severe) at baseline. Patients were randomized 2:1 to receive HP/TAZ or vehicle lotion once daily for 8 weeks, with a 4-week posttreatment follow-up. Pooled post hoc analyses were conducted in patients with BSA involvement of 3% to 5% at baseline and patients with BSA involvement of 3% to 5% and DLQI of <5 at baseline. Efficacy measures were treatment success (≥2-grade reduction in IGA and score of 0 [clear] or 1 [almost clear]) and success rates in reductions of plaque elevation and scaling (≥2-grade improvements from baseline). Treatment-emergent adverse events (TEAEs) were also evaluated.

Results: Of 418 patients at baseline, 232 had BSA involvement of 3% to 5% and 84 had BSA involvement of 3% to 5% and DLQI of <5. Patients with BSA involvement of 3% to 5% who received HP/TAZ had significantly higher rates of treatment success at week 8 vs those receiving vehicle (42.7% vs 11.4%; $P<0.001$). Treatment success rates at week 8 for those with BSA involvement of 3% to 5% and DLQI of <5 were numerically higher but not statistically significant with HP/TAZ vs vehicle (41.6% vs 14.7%; $P=0.068$). At week 8, HP/TAZ vs vehicle was associated with significantly higher success rates in reductions of plaque elevation (56.0% vs 19.4%; $P<0.001$) and scaling (62.7% vs 25.6%; $P<0.001$) in patients with BSA involvement of 3% to 5%. Comparable results were observed at week 8 in those with BSA involvement of 3% to 5% and DLQI of <5 (plaque elevation: 59.6% vs 28.4%; $P=0.016$; scaling: 63.2% vs 26.0%; $P=0.016$). Overall TEAEs occurred more in patients receiving HP/TAZ vs vehicle through week 8 in both subgroups; rates of serious TEAEs and discontinuations were low (≤5%).

Conclusions: HP/TAZ was associated with higher efficacy rates vs vehicle and was generally well tolerated in patients with lower BSA involvement who are candidates for topical psoriasis therapy.

Reference: 1. DUOBRII [package insert]. Bausch Health US, LLC; 2020. 2. Elmets et al. *J Am Acad Dermatol.* 2021;84(2):432-470.

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Skin deposition of tazarotene with 0.045% lotion versus 0.1% cream

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Introduction: Acne can be treated with topical retinoids such as tazarotene (TAZ). A lower-dose TAZ 0.045% lotion was developed using polymeric emulsion technology, allowing for rapid/uniform distribution of active ingredients. This lotion—with less than half the concentration of TAZ as 0.1% gel, cream, and foam—may reduce local skin reactions that affect tolerability of 0.1% formulations in some patients. The objective of this study was to compare skin deposition of TAZ after application of 0.045% lotion and 0.1% cream formulations, using a novel tape-stripping plus liquid chromatography-mass spectrometry (LC-MS) analysis technique.

Methods: Healthy adults with normal skin and none-to-minimal hair on ventral forearms were eligible to participate. TAZ 0.045% lotion and 0.1% cream were applied to two 1.5"x1.5" squares on opposite forearms (~0.1 g of product at each site). After 3 and 6 hours, 21 tape strips were used to sample the skin from one application site on each forearm (first strip discarded); each strip sampled a deeper skin layer, through stratum corneum into lower epidermis and superficial dermis. Mean TAZ levels from even-numbered strips were evaluated using LC-MS. Assessments included percent recovery of the applied TAZ dose and concentration of TAZ recovered at each tape strip.

Results: Ten female Caucasian participants aged 19-59 years completed the study. Ten even-numbered tape strips were obtained at both 3 and 6 hours for each TAZ formulation. Percent recovery of the total applied TAZ dose from even-numbered strips was greater for 0.045% lotion versus 0.1% cream (6 hr: 15.5% vs 13.8%, respectively); this may be due to the polymeric emulsion technology used to develop the lotion. TAZ concentration was highest at the skin surface for both formulations, though concentrations were approximately 2-fold higher for cream than lotion at both superficial and deep skin layers (6 hr: strip 2, 1.62 vs 0.82 µg/mL; strip 20, 0.18 vs 0.09 µg/mL). However, absolute differences in TAZ concentrations between formulations drastically decreased in progressively deeper skin layers, from 0.8 µg/mL at tape strip 2 to 0.09 µg/mL at tape strip 20 (6 hr post-application). Similar trends were observed with the 3-hour strips.

Conclusion: Higher percent drug recovery with TAZ 0.045% lotion versus 0.1% cream may be due to the polymeric emulsion technology used in the lotion. Overall, most TAZ remained on the skin surface, with 2-fold higher TAZ levels on strip 2 with cream versus lotion. These results provide important context for findings from a 12-week study of moderate-to-severe acne (n=210), in which TAZ 0.045% lotion had comparable efficacy but fewer adverse events than 0.1% cream.[1] Small differences between lotion and cream in TAZ deposition at deeper skin layers may not be clinically relevant to efficacy; however, lower-dose 0.045% lotion may minimize TAZ exposure at the skin surface versus 0.1% cream, potentially contributing to a more favorable tolerability profile.

Funding: Ortho Dermatologics.

Reference:
1. Tanghetti EA, et al. *J Drugs Dermatol.* 2019;18(6):542-548.

Efficacy and Safety of Crisaborole in Patients With Mild-to-Moderate Atopic Dermatitis With and Without Comorbid Allergies or Asthma

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Introduction: Crisaborole ointment, 2%, is a nonsteroidal anti-inflammatory phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate atopic dermatitis (AD). This post hoc pooled analysis of the phase 3 studies CrisADe CORE 1 (NCT02118766) and CORE 2 (NCT02118792) was conducted to evaluate the efficacy and safety of crisaborole in patients with mild-to-moderate AD with or without comorbid asthma/allergies.

Methods: Patients aged ≥2 years with mild-to-moderate AD were randomly assigned 2:1 to receive twice-daily crisaborole or vehicle for 28 days. Outcomes were Investigator's Static Global Assessment (ISGA) success (clear [0] or almost clear [1] with a ≥2-grade improvement from baseline) and ISGA clear/almost clear at day 29. Patients were stratified by history of asthma/allergies (which included but was not limited to allergic rhinitis, food, and other allergies).

Results: Crisaborole and vehicle were received by 585 and 304 patients, respectively, with asthma/allergies (mean age, 12.4 vs 12.1 years; moderate disease, 63.6% vs 66.1%) and by 431 and 202 patients, respectively, without asthma/allergies (mean age, 12.2 vs 12.1 years; moderate disease, 58.2% vs 55.5%). ISGA success rate (95% CI) at day 29 was 29.4% (25.5%-33.3%) and 20.1% (15.3%-24.9%), respectively, in patients with asthma/allergies (difference, *P*=0.003) and 35.8% (31.1%-40.5%) and 24.6% (18.1%-31.0%), respectively, in patients without asthma/allergies (difference, *P*=0.006). Rate of ISGA clear or almost clear at day 29 was 48.4% (44.1%-52.8%) and 32.0% (26.5%-

37.5%), respectively, with asthma/allergies (difference, *P*<0.0001) and 52.4% (47.6%-57.3%) and 40.6% (32.4%-48.7%), respectively, without asthma/allergies (difference, *P*=0.014). No new safety concerns were identified.

Conclusion: Crisaborole is efficacious and safe in treating patients with mild-to-moderate AD regardless of a history of asthma/allergies.

Dupilumab Provides Clinically Meaningful Improvement in Atopic Dermatitis (AD) Signs, Symptoms, and Quality of Life in Children With Severe AD: Results From the LIBERTY AD PEDS Phase 3 Clinical Trial

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Background: Patients with atopic dermatitis (AD) suffer from a multidimensional disease burden. We report clinically meaningful improvements in AD signs, symptoms, and quality of life in children treated with FDA-approved doses of dupilumab.

Methods: In LIBERTY AD PEDS phase 3 trial (NCT03345914), children aged 6–11 years were randomized to dupilumab 300mg every 4 weeks (300mg-q4w, loading dose 600mg), 100mg/200mg-q2w (loading dose 200mg/400mg), or placebo; with concomitant medium-potency topical corticosteroids (TCS). We evaluated the proportion of patients reaching a composite endpoint at Week (Wk) 16 of achieving: ≥ 50% improvement in Eczema Area and Severity Index (EASI-50); and ≥ 3-point improvement in Peak Pruritus Numerical Rating Scale (PP-NRS) score; and ≥ 6-point improvement in Children's Dermatology Life Quality Index (CDLQI) from baseline.

Results: This analysis included 243 patients (<30kg: 300mg-q4w+TCS/placebo+TCS; ≥30kg: 200mg-q2w+TCS/placebo+TCS, n=61/61/59/62). In both the 300mg-q4w and 200mg-q2w dupilumab dosing regimens, almost half of the children treated with dupilumab achieved all 3 clinically meaningful endpoints (objective and patient-reported) at Wk16 (49.2%/9.8%, 300mg-q4w/placebo <30kg and 47.5%/8.1% 200mg-q2w/placebo ≥30kg; *P*<0.0001 for both). A significantly higher proportion of patients achieved EASI-50 or ≥ 3-point improvement in PP-NRS or ≥ 6-point improvement in CDLQI at Wk16 vs placebo (95.1%/62.3%, 300mg-q4w/placebo <30kg and 94.9%/59.7% 200mg-q2w/placebo ≥30kg; *P*<0.0001 for both). Safety profile was consistent with the known dupilumab safety profile in adult and adolescents.

Conclusion: Dupilumab+TCS provides clinically meaningful and statistically significant improvements in AD signs (EASI-50), symptoms (PP-NRS), and quality of life (CDLQI) in children aged 6–11 years with severe AD.

Dupilumab Provides Early and Sustained Clinically Meaningful Responses in a Phase 3 Trial in Adolescents with Inadequately Controlled Moderate-To-Severe Atopic Dermatitis: Results from the Overall Population and in a Subgroup of Patients Not Achieving IGA Scores Of 0/1

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Background: A potentially useful evaluation of the effectiveness of treatment for inadequately controlled moderate to-severe atopic dermatitis (AD) may include clinically relevant improvement in various domains of AD including signs, symptoms, and health-related quality of life (QoL).

Objective: To determine the proportion of patients with a clinically meaningful response in AD signs, symptoms, and QoL following 16-week dupilumab treatment in the overall adolescent population, and in a subgroup not achieving Investigator's Global Assessment (IGA) scores of 0/1 (clear/almost clear) at Week 16 (Wk16) in a randomized, double-blinded, placebo-controlled, phase 3 trial (LIBERTY AD ADOL: NCT03054428).

Methods: Adolescents ≥12 to <18 years with inadequately controlled moderate to-severe AD were randomized 1:1:1 to subcutaneous dupilumab every 4 weeks (q4w; 300mg), every 2 weeks (q2w; 200/300mg), or placebo for 16 weeks. Clinically meaningful responses were defined as ≥50% improvement in Eczema Area and Severity Index, or ≥3-point improvement in weekly-averaged Peak daily Pruritus Numerical Rating Scale (NRS), or ≥6-point improvement in Children's Dermatology Life Quality Index from baseline through Wk16. A composite endpoint was defined as a clinically meaningful response in ≥1 of the above 3 endpoints.

Results: Overall, 251 patients were randomized to dupilumab q4w (n=84), dupilumab q2w (n=82), and placebo (n=85). At Wk16, significantly more patients receiving dupilumab achieved the composite endpoint vs. placebo (q4w/q2w vs. placebo: 63.1%/80.5% vs. 23.5% [*P*<0.0001 for both]). Among randomized patients, 82.1% (q4w), 75.6% (q2w), and 97.6% (placebo) patients did not achieve IGA 0/1 at Wk16 (IGA >1 subgroup). In this subgroup, significantly more patients receiving dupilumab achieved the composite endpoint vs. placebo (q4w/q2w vs. placebo: 55.1%/74.2% vs. 21.7% [*P*<0.0001 for both]) at Wk16. Clinically meaningful responses in both populations were seen as early as Week 2 after first dose. Compared with placebo, NRS scores (least-squares mean percent change) improved as early as Day 5 for q2w

(*P*=0.0265) and Day 6 for q4w (*P*=0.0095) in the overall population, and as early as Day 3 for q2w (*P*=0.0265) and q4w (*P*=0.0219) in the IGA >1 subgroup. Dupilumab was generally well tolerated with an acceptable safety profile similar to that seen in the adult AD population.

Conclusion: A majority of adolescents treated with dupilumab, including those with IGA >1 at Wk16, demonstrated early, progressive, and sustained clinically meaningful responses in ≥1 key AD domain (signs, symptoms, and QoL) compared with placebo.

Rapid and Sustained Improvement in Itch in Children Aged 6–11 Years With Severe Atopic Dermatitis (AD) Treated With Dupilumab: Analysis From the LIBERTY AD PEDS Phase 3 Trial

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Background: In LIBERTY AD PEDS phase 3 trial (NCT03345914) in children with severe AD, dupilumab significantly improved AD signs and symptoms. We assess time to onset of improvement in pruritus in a subset of children treated with FDA-approved doses of dupilumab.

Methods: Children aged 6–11 years were randomized to dupilumab 300mg every 4 weeks (300mg-q4w, loading dose 600mg), 100mg/200mg-q2w (loading dose 200mg/400mg), or placebo, with concomitant medium-potency topical corticosteroids (TCS). This analysis evaluated change from baseline in daily and weekly Peak Pruritus Numerical Rating Scale (PP-NRS) scores up to Week 16.

Results: This analysis included 243 patients treated with FDA-approved doses of dupilumab, or placebo (< 30kg: 600mg loading dose then 300mg-q4w+TCS/placebo+TCS; ≥ 30kg: 400mg loading dose then 200mg-q2w+TCS/placebo+TCS, n=61/61/59/62). The percent decrease in daily PP-NRS score (SE) from baseline of dupilumab+TCS vs placebo+TCS was significant, as early as Day 8 in the q4w group after a single dose (−13.8% [2.9] vs −5.1% [2.9]; $P < 0.05$) and Day 16 in the q2w group (−22.1% [3.4] vs −12.6% [3.3]; $P < 0.05$). At Week 16, mean percent change from baseline (SE) in weekly PP-NRS score in the q4w group vs placebo+TCS was −55.0% (4.0) vs −26.6% (4.3) ($P < 0.0001$) and −58.3% (4.0) vs −25.3% (3.9) ($P < 0.0001$) in the q2w group vs placebo+TCS. Safety profile was consistent with the known dupilumab safety profile.

Conclusions: Dupilumab + TCS treatment provided rapid and sustained improvement in itch intensity and frequency in children aged 6–11 years with severe AD.

Design of a prospective, multicenter, randomized, evaluator-blinded study to evaluate the efficacy and safety of topical minocycline foam 4% with oral isotretinoin for the treatment of moderate-to-severe acne vulgaris

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Introduction: Acne vulgaris is a ubiquitous disease of the pilosebaceous unit frequently treated with antibiotics, retinoids, or combination therapy. FMX101 is a topical lipophilic foam containing 4% minocycline, a tetracycline antibiotic with antibacterial and anti-inflammatory properties. Phase 3 clinical trials have demonstrated the safety, efficacy, and tolerability of FMX101 for the treatment of moderate-to-severe acne. Oral isotretinoin is an established treatment for severe acne with a safety profile that requires careful monitoring. The combination of these 2 US Food and Drug Administration–approved treatments may offer an improved treatment option for the long-term management of acne. The objective of this study was to evaluate the efficacy, safety, and tolerability of concomitant use of FMX101 foam and oral isotretinoin compared with oral isotretinoin only in the treatment of patients with moderate-to-severe acne. We also evaluated the efficacy of FMX101 foam as a maintenance therapy following discontinuation of oral isotretinoin.

Methods: A prospective, multicenter, randomized, evaluator-blinded study will be conducted. Approximately 30 patients (aged ≥12 years) of either sex with moderate-to-severe acne per Investigator Global Assessment (IGA) scores (IGA = 3 or 4) will be randomly assigned (1:1) to receive 20 weeks of concomitant FMX101 4% topical minocycline foam and once-daily oral isotretinoin treatment (0.5 mg/kg/day for the first 4 weeks, 1.0 mg/kg/day for the following 16 weeks) or oral isotretinoin treatment alone. After this 20-week treatment period, all patients will receive FMX101 for an additional 24-week maintenance phase. FMX101 foam will be applied once daily to the full face and other acne-affected areas. After the baseline visit, patients will return for efficacy and safety evaluations at weeks 1 and 2, and then every 4 weeks for the remainder of the study. Patients who report any treatment-emergent adverse event (TEAE) will return for a safety evaluation 4 weeks following the maintenance phase. The coprimary efficacy endpoints are the percent change from baseline in inflammatory and noninflammatory lesion counts, and the proportion of patients with IGA treatment success (dichotomized as yes/no). IGA treatment success is defined as an IGA score of 0 or 1, and at least a 2-grade improvement from baseline. Safety evaluations will include TEAEs, physical examinations, vital signs, and local skin tolerability assessments.

Conclusion: We hypothesize that maintenance therapy with FMX101 topical foam following oral isotretinoin will optimize long-term disease control, with a favorable safety profile. These results will provide insights on sequence dosing of oral isotretinoin and FMX101 in the long-term management of acne.

Bimekizumab efficacy in patients with moderate to severe plaque psoriasis during the randomized withdrawal and retreatment phase of BE READY, a phase 3 trial

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Introduction: Patients with plaque psoriasis often report gaps in biologic treatment, due to reasons including invasive surgery, infection, or changes to insurance.[1,2] We report bimekizumab efficacy following randomized withdrawal from treatment and retreatment in BE READY.[3]

Methods: Patients with moderate to severe plaque psoriasis were randomized 4:1 to bimekizumab 320 mg every 4 weeks (Q4W) or placebo.[3] At Week 16, bimekizumab-treated PASI 90 responders were re-randomized 1:1:1 to bimekizumab 320 mg Q4W, bimekizumab 320 mg every 8 weeks (Q8W), or placebo through Weeks 16–56 (randomized withdrawal). Patients who relapsed during randomized withdrawal entered a 12-week escape arm and were retreated with bimekizumab 320 mg Q4W. Relapse was defined as response lower than PASI 75. Missing data were imputed as non-response.

Results: At Week 16, 311 bimekizumab-treated patients (89.1%) achieved PASI 90 and were re-randomized: 106 to bimekizumab Q4W, 100 to bimekizumab Q8W, 105 to placebo. At Week 56, PASI 90 was maintained by 86.8% and 91.0% patients re-randomized to bimekizumab Q4W and Q8W, respectively. Median time to loss of PASI 75 response (relapse) for patients re-randomized to placebo was 28 weeks after re-randomization (32 weeks after last bimekizumab dose). 67 patients re-randomized to placebo relapsed, entering the bimekizumab escape arm. Of these, 65.7% achieved PASI 90 after 4 weeks' escape treatment, increasing to 88.1% after 12 weeks' escape treatment; DLQI 0/1 responder rates were 58.2% and 82.1% after 4 and 12 weeks' escape treatment, respectively.

Conclusions: For patients re-randomized to placebo, median time to relapse was 28 weeks. Following relapse, patients showed rapid recapture of response on retreatment with bimekizumab during 12-weeks' escape treatment.

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2. Wu JJ et al. *J Med Econ* 2019;22:365–371;
3. Gordon KB et al. *Lancet* 2021;397:475–86.

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MG: Investigator, speaker, consultant or advisory board member for AbbVie, Amgen, Akros, Arcutis, Bausch Health, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Galderma, GSK, Janssen, Kyowa Kirin, MedImmune, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and UCB Pharma.

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Bimekizumab response maintenance up to 1 year in patients with moderate to severe plaque psoriasis: Pooled results from three phase 3 trials

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Introduction: Given the chronic nature of plaque psoriasis, it is important to maintain treatment efficacy over time. Here, we report maintenance of response over 1 year pooled from three phase 3 studies in patients with moderate to severe plaque psoriasis who achieved complete or near complete skin clearance after 16 weeks of bimekizumab treatment.

Methods: Data were pooled from BE VIVID, BE READY, and BE SURE.[1–3] Included patients were randomized to receive bimekizumab 320 mg every 4 weeks (Q4W) to Week 16, then either continued to receive bimekizumab Q4W (Q4W/Q4W) or switched to bimekizumab 320 mg every 8 weeks (Q4W/Q8W). We report PASI 90, IGA 0/1, and PASI 100 responses at Week 52 among Week 16 responders. Missing data were imputed as non-response.

Results: Of the 989 patients randomized to bimekizumab 320 mg Q4W in these studies, the majority achieved complete or near complete skin clearance at Week 16 (PASI 90: 87.5%; IGA 0/1: 87.5%; PASI 100: 62.7%). Among Week 16 PASI 90 responders in the Q4W/Q4W (N=516) and Q4W/Q8W (N=237) groups, 89.9% and 90.3% maintained PASI 90 at Week 52, respectively. Among Week 16 IGA 0/1 responders in the Q4W/Q4W (N=511) and Q4W/Q8W (N=234) treatment groups, 87.5% and 91.5% maintained IGA 0/1 at Week 52. Among Week 16 PASI 100 responders in the Q4W/Q4W (N=355) and Q4W/Q8W (N=182) groups, 83.1% and 88.5% maintained PASI 100 at Week 52.

Conclusions: A high proportion of patients who achieved complete or near complete skin clearance after 16 weeks of bimekizumab treatment maintained their responses through Week 52, regardless of maintenance dosing schedule (Q4W or Q8W).

References:

1. Reich K et al. *Lancet* 2021;397:487–98;
2. Gordon KB et al. *Lancet* 2021;397:475–86;
3. Warren RB et al. *N Engl J Med* 2021 Apr [Epub ahead of print].

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Bimekizumab short-term and longer-term infection rates in patients with moderate to severe plaque psoriasis: Analysis of pooled data from eight phase 2/3 clinical trials

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Introduction: Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits both interleukin (IL)-17A and IL-17F.[1] In this study, we report 16-week infection rates pooled across three phase 3 trials in patients with moderate to severe plaque psoriasis receiving bimekizumab compared with patients receiving adalimumab, ustekinumab, or placebo and longer-term infection rates pooled across eight phase 2/3 trials in bimekizumab-treated patients with moderate to severe plaque psoriasis.

Methods: Short-term infection rates were evaluated for bimekizumab, adalimumab, ustekinumab, and placebo through 16 weeks in three phase 3 trials.[2–4] Longer-term rates were evaluated for bimekizumab across eight phase 2/3 completed double-blinded and ongoing open-label trials.[2–9]

Results: Through Week 16 of three phase 3 trials, 989 patients received bimekizumab, 159 received adalimumab, 163 received ustekinumab, and 169 received placebo, representing 306.0 patient-years (PY), 48.8 PY, 50.1 PY, and 51.6 PY, respectively. Longer-term data (up to 670 days of exposure) included 1,789 bimekizumab-treated patients (1,830.4 PY). Through Week 16, infections occurred in 37.6% of bimekizumab-treated versus 39.0%, 20.9%, and 22.5% of adalimumab-, ustekinumab-, and placebo-treated patients; serious infections (SIs) occurred in 0.3% versus 0.0%, 1.2%, and 0.0%. The most common infections with bimekizumab were nasopharyngitis (9.2%) and oral candidiasis (7.6%). In the longer term, across eight phase 2/3 trials, infection and SI rates with bimekizumab were 117.8/100 PY and 1.4/100 PY, respectively, comparable with Week 16 (infections: 150.7/100 PY; SIs: 1.0/100 PY). The most common SI (>2 events) was cellulitis (0.2/100 PY). The longer-term rate of oral candidiasis was 16.4/100 PY. The vast majority of oral candidiasis events were mild to moderate (99.4%); <1% led to discontinuation. No cases of systemic fungal infection and no cases of active tuberculosis occurred.

Conclusion: Week 16 infection rates with bimekizumab were comparable with those for adalimumab and higher than with ustekinumab or placebo; rates with bimekizumab did not increase with exposure. Infections with bimekizumab were predominantly non-serious. Oral candidiasis infections were predominantly mild to moderate and did not lead to discontinuation.

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8. https://clinicaltrials.gov/ct2/show/NCT03025542;
9. https://clinicaltrials.gov/ct2/show/NCT03230292.

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Speed of clinical response and improvement in psoriasis with bimekizumab: Pooled results from the multicenter, randomized, double-blinded phase 3 BE VIVID, BE READY and BE SURE trials

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Introduction: Speed of psoriasis symptom improvement is one of several attributes valued by patients and is an important treatment goal.[1] Here, we examine efficacy and impact on quality of life in patients with moderate to severe plaque psoriasis receiving bimekizumab versus comparators within the first 16 weeks of treatment.

Methods: Data were pooled from the BE VIVID, BE READY, and BE SURE phase 3 trials[2–4] comparing treatment through Week 16 with bimekizumab 320 mg every 4 weeks versus adalimumab, ustekinumab, and/or placebo. Up to Week 16, median time to (Kaplan-Meier estimates, where >16 weeks was not reported) and proportions of patients achieving PASI 75, PASI 90, PASI 100, IGA 0/1, and DLQI 0/1 were assessed (non-responder imputation).

Results: A total of 1,480 patients were randomized (bimekizumab: 989; ustekinumab: 163; adalimumab: 159; placebo: 169). Median times to PASI 100, IGA 0/1, and DLQI 0/1 response were shorter with bimekizumab versus ustekinumab and adalimumab, respectively (PASI 100: 12.1 weeks versus >16 and >16; IGA 0/1: 4.3 weeks versus 12.1 and 12.1; DLQI 0/1: 8.1 weeks versus >16 and 12.3).

At Week 4, the proportion of patients achieving PASI 75 was highest in bimekizumab after one dose as compared to ustekinumab/adalimumab/placebo: 76.4% versus 15.3%/31.4%/1.8% respectively; similar trends were seen for PASI 90 (42.9% versus 3.1%/5.0%/1.2%), PASI 100 (16.5% versus 1.2%/1.3%/1.2%), and DLQI 0/1 (39.4% versus 11.0%/25.8%/6.5%). Results with bimekizumab versus ustekinumab/adalimumab/placebo were consistent at Week 16 for PASI 75 (93.4% versus 73.0%/69.2%/4.7%), PASI 90 (87.5% versus 49.7%/47.2%/3.0%), PASI 100 (62.7% versus 20.9%/23.9%/0.6%), and DLQI 0/1 (68.9% versus 42.3%/46.5%/8.9%).

Conclusions: Bimekizumab demonstrated faster skin clearance and greater clinical benefit compared to ustekinumab, adalimumab and placebo.

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2. Reich K et al. Lancet 2021;397:487–98;
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4. Warren RB et al. N Engl J Med 2021 Apr [Epub ahead of print].

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Safety and Efficacy of VP-102 (Cantharidin, 0.7% w/v) in the Treatment of Molluscum Contagiosum by Body Region and Visit

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Background: VP-102 is proprietary drug-device combination product containing a controlled topical formulation with cantharidin (0.7% w/v) and has completed Phase 3 trials for the treatment of molluscum contagiosum (molluscum). Post-hoc analyses determined the pooled safety and efficacy of VP-102 at each visit by molluscum lesion body region where lesions were present at baseline, segmented by head/neck, chest/

abdomen, upper extremities, back/buttocks, groin, and lower extremities.

Methods: Subjects ≥ 2 years of age with a clinical diagnosis of molluscum were enrolled in two Phase 3 trials with identical protocols and randomized in a 3:2 ratio to topical administration of VP-102 or vehicle applied to all baseline and new molluscum lesions once every 21 days until clear, or up to a maximum of 4 applications. Lesion counts and body regions were recorded at days 1 (baseline), 21, 42, 63, and 84 (the end of study (EOS) visit). The efficacy population included subjects with lesions in the specific body regions at baseline. Efficacy was measured by the percentage of subjects with complete clearance of lesions in each location by visit. Lesions could be present in more than one body region, and individual lesions were not tracked. Targeted adverse events (AEs) were documented throughout the study with a focus on local skin reactions. The safety population included subjects who received at least one treatment of study drug.

Results: Subjects had lesions in the following regions at baseline: head/neck (n=77 VP-102, n=53 vehicle), upper extremities (n=179, 131), lower extremities (n=186, 141), back/buttocks (n=117, 91), groin (n=28, 25), or chest/abdomen (n=142, 118). The percentage of subjects with complete clearance of all lesions was statistically significantly higher in the VP-102 group than vehicle in all body regions at the EOS visit. Clearance of Head/neck, chest/abdomen, back/buttocks, and upper extremities were statistically significantly higher than vehicle beginning after the first visit through the EOS visit (all $p<0.05$). Clearance rates of the lower extremities were significantly higher for VP-102 vs vehicle beginning at day 42, and in the groin beginning at day 63 through the EOS visit ($p<0.05$). All clearance rates will be presented in the poster. Incidence of targeted AEs were consistent across regions for the VP-102 group.

Conclusions: Treatment of molluscum with VP-102 showed statistically significantly higher efficacy of percentage of subjects with complete clearance vs. vehicle across all body locations, though different body regions may require a different number of treatments for complete clearance. The VP-102 group showed similar incidence of AEs across all body regions.

The Hidden Impact of Molluscum Contagiosum: Survey of Caregivers' Experiences with Diagnosis and Management

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Objective: Molluscum contagiosum (molluscum) is a common pediatric viral skin infection. Molluscum can last for months to years and cause itching and pain. The experience in caring for a child with molluscum largely remains a mystery, with few studies published on the topic. This online survey aimed to collect caregivers' views on their experiences with molluscum infection in their children.

Methods: Parents, caregivers, and/or legal guardians of children (ages 3-16 years) diagnosed with molluscum in the past 4 years were recruited to answer a 15-minute paid online survey. Survey questions inquired about the type of health care provider (HCP) consulted, diagnosis, treatment, and how severely molluscum impacted the caregiver and the child.

Results: Respondents (n=150) were mostly Caucasian (85%), 25-44 years of age (87%), and had at least one child with an active infection (75%). Median household size was 4 people. The median age of children in the home was 8 years. Most respondents saw at least 2 types of HCPs for their child's molluscum. Diagnosis was completed by Pediatrics (49%), Family Practice (37%), Dermatology (34%), Infectious Disease (23%), and/or Emergency Room (21%). Spread of molluscum to ≥ 1 child in the household was reported in 60% of caregivers. Most caregivers were offered treatment options by the health care provider (61%) vs. allowing the disease to remit on its own (39%). Most caregivers reported moderate to major impact on their lives (62%), 70% agreed with the statement that molluscum kept their child away from doing things they love, and 62% agreed they worried what others thought of their child having molluscum. Many respondents (47%) considered squeezing or removing lesions themselves at home and 31% utilized this strategy. The most common approaches to treatment were home remedies (43%) and molluscum treatments purchased from Amazon.com or a drug store with no Rx required (41%), followed by cryosurgery (41%), cantharidin (39%), and curettage (31%). The average number of treatments used was 2.36.

Conclusions: Results indicate that molluscum patients receive diagnoses from many HCP types, often visiting more than one HCP. Many patients do not receive treatment, and those that do receive treatment are likely to use more than one modality in attempt to clear the infection. Caregivers were likely to attempt to try at-home remedies or use unproven/unapproved remedies, as well as attempt to disrupt lesions themselves, creating opportunities for autoinoculation and spread of the infection. Spread in the household was common. A moderate to high impact on quality of life for caregivers and an impact on activities for their children with molluscum was reported. This suggests that while physically benign, molluscum has an emotional impact patients and their caregivers, with concern over a negative social stigma.

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