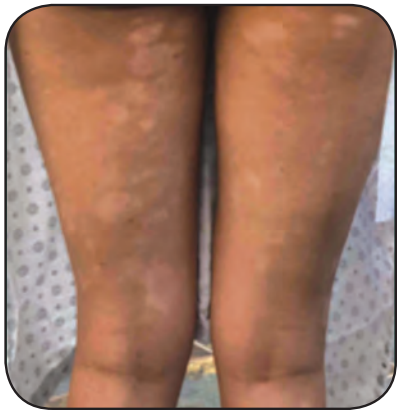
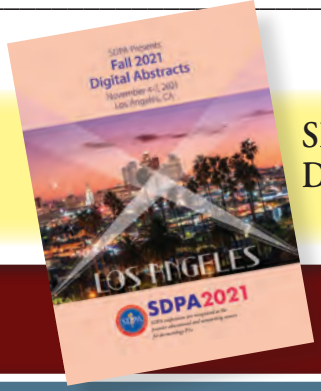
VOLUME 15 • NUMBER 4 • FALL 2021

JDPA

Journal of Dermatology for Physician Assistants





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JDPA/Journal of Dermatology for Physician Assistants (ISSN 1938-9574) is published quarterly (4 issues per volume, one volume per year) by the Society of Dermatology Physician Assistants (SDPA), 300 N. Washington Street, Suite 407, Alexandria, VA 22314. Volume 15, Number 4, Fall 2021. One-year subscription rates: $40 in the United States and Possessions. Single copies (prepaid only): $10 in the United States (Include $6.50 per order plus $2 per additional copy for US postage and handling). Periodicals postage rate paid at New York, NY 10001 and additional mailing offices.

POSTMASTER: Send address changes to Society of Dermatology Physician Assistants, Inc., 300 N. Washington Street, Suite 407, Alexandria, VA 22314
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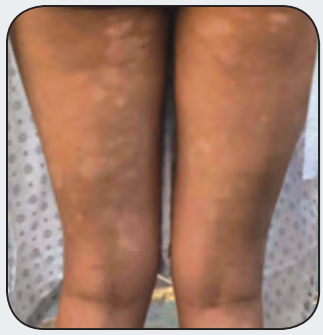

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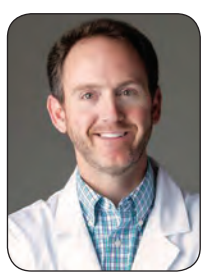
Celebrating the Advancement of Our Profession

It goes without question that our world and its people have endured a great deal of changes and challenges throughout this ongoing pandemic. We have witnessed entire industries shift and change their methods overnight. I remain in total awe of the fact that we have seen firsthand the marvel that is science. We have watched as teams of dedicated scientists and researchers have developed a vaccine to protect us against Covid-19, and they have done that in less than a year's time frame. Let that sink in. We are living in a time of great scientific advancement.

As a PA, I feel we are also living in a time of great advancement for our profession. I have always been grateful for the early PA pioneers who came before us and laid the framework for our profession. Each generation of PAs that followed have then built upon the previous generation's work in educating patients on the role of PAs and advancing our profession. And here we are today, living in this period of time with a recently approved change to our title and ongoing individual state legislation changes advancing PAs into independent practices. These processes have not occurred overnight and did not occur due to one or two individuals. It is such an impressive time to be working as a PA and knowing that your combined efforts, collaborating and working with others who are equally as passionate and energetic, are helping with the forward advancement of our profession.

I am extremely proud to be a part of such a network of volunteers who are willing to share information and help one another to keep our momentum moving forward. The network of dedicated elected PA leaders and appointed committee members within the SDPA is one that has continued to help advance our specialty and profession forward year after year. When we step back and take inventory of what those volunteers have helped us to develop, it is truly impressive! The SDPA continues to advance thanks in large part to the people who stepped forward to lend a hand and make things happen.

As we continue to advance as a society, as independent practicing PAs, and as members of the SDPA, I continue to be thankful to be part of this wonderful group of healthcare workers and am especially thankful and grateful to be a PA during this incredible period in time. If you have ever considered joining in to help with this advancement, now is the time to do so! Feel free to reach out to me (haydentm@lemoyne.edu) at any time to discuss how you can get started and get involved!



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

Alabama Society of Dermatology Professionals (ASDP) Annual Fall Meeting 2021
November 12-13, 2021
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2022 American Academy of Dermatology Annual Meeting
March 25-29, 2022
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2022 New Wave Dermatology Southeast Regional Conference: An Educational Symposium for the Future of Physician Assistants
April 28, 2022 - May 1, 2022
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June 16–19, 2022
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FROM THE PRESIDENT'S DESK:

Inclusion and Encouragement, Collaboration and Communication are Crucial to Successful Leadership

Change is inevitable, but how we adapt to changes in life can determine whether we can move forward. Sometimes our reaction is to wonder why change is needed if things are perfect the way they are. But are they "perfect?" What is ideal for one person doesn't mean it is suitable for all. What worked yesterday may not even be considered for today. We must learn to adapt and pivot quickly; otherwise, we will be left behind. Trust me; I have been there trying to keep up with social media, work, family, and this thing called life! Some days I feel left behind, and others think I am way ahead of the game. But, in the end, I keep going. You have to!

It's exciting to see the landscape of opportunities broaden for Dermatology PAs. However, one thing remains the same—every one of us is an ambassador for the profession. If we all continue to move forward together, the road will widen, and the opportunity path to growth will be well established for the future Derm PAs who will continue to do the same. Sure, there will be bumps in the road because, if it were easy, every one of us would be doing it 24/7. However, if we all pitch in, it will become easier to get the message across of everything we can do and much more. The leaders of any organization are not the only ones promoting our profession; all of you who go to work as a Derm PA do so daily. So, make sure your voice is heard loud and clear that you are proud to be a PA, that you are an integral part of the Dermatology Team, and that you matter.

What I have learned throughout my leadership years is that collaboration and communication are crucial to success. Most importantly, inclusion. Inclusion of all, no matter what level of leadership they are at. Leadership is not nor ever will be a popularity contest or game. In addition, appreciation of volunteers and staff is essential to keep the morale up. Even if it is a quick text message saying, "I appreciate you," "Keep up the good work," or a simple "Hello, how are you doing today?" can make a huge difference. This type of gesture also makes a huge difference at work as I speak to many colleagues who feel "invisible" or unappreciated. Maybe everyone should be taught the ethics and etiquette of being a team player because, in the end, it is for all the patients we care about.

Leadership comes in all forms (i.e., time commitment, personality, talent). Having an extensive network to bring it together keeps it growing and makes it more accessible for all involved. That is why we need you. The SDPA needs your uniqueness, time (whatever you have to give), and ideas for us to grow. Finally, please remember, we all need encouragement to open our own leadership door. People sometimes need an extra "push"

to take it to the next level, which is okay. The person to offer that extra push to a future leader might be you! Remember that.

The SDPA Leadership Summit was 100 percent focused on Derm PAs. We have learned to make positive habits in our daily lives by being goal-oriented, embracing change, accepting responsibility, complementing, and never stopping learning. Most importantly, make sure you listen and understand without losing either your self-confidence or temper.

Keep in mind that you are not only members of the SDPA, but you are goodwill ambassadors for the profession. You represent the profession every single day. You make the difference in access to patient care, research, and education. Be very proud of that.

Warm regards,

Renata Block

Renata Block, MMS, PA-C
President SDPA

Hypopigmented Mycosis Fungoides in Younger Patients: *A Mimicker of Common Hypopigmented Inflammatory Rashes*

By Candice E. Macari, DMSc, MSPAS, MPH, PA-C

ABSTRACT

Hypopigmented mycosis fungoides (HMF) is a rare type of cutaneous T-cell lymphoma (CTCL), a non-classic variant among up to 50 variants of mycosis fungoides (MF), that typically affects younger individuals in the second to fourth decades of life of darker skin types. The presenting cutaneous findings of HMF can be mistaken for and mimic other commonly seen hypopigmented skin disorders and misdiagnosed by an untrained eye in the dermatologic and general practice settings. MF has many different variants, and affects both children and adults. For the purpose of this article, the discussion will be limited to HMF specifically presenting in younger patients. With limited literature on HMF commonly affecting the younger generations, knowledge of how to diagnose and treat this cutaneous malignancy is lacking among clinicians. The goal of this CME article is to provide more awareness to clinicians on this rare form of CTCL, thus improving patient care through early detection and treatment in this patient population.

KEYWORDS

Hypopigmented mycosis fungoides, mycosis fungoides, cutaneous T-cell lymphoma, young patients, prognosis, overall survival, hypopigmentation, lymphoma, pediatric lymphomas, phototherapy.

» CME

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Learning Objectives:

1. *Discuss the clinical and physical presentations of hypopigmented mycosis fungoides compared to commonly seen hypopigmented rashes.*
2. *Review current workup and treatment for hypopigmented mycosis fungoides.*
3. *Discuss delayed diagnosis, long-term clinical prognosis, and recurrence rate with hypopigmented mycosis fungoides.*
4. *Describe histopathological findings*

INTRODUCTION

Hypopigmented mycosis fungoides (HMF), is an extremely rare variant of mycosis fungoides (MF), a cutaneous T-cell lymphoma (CTCL).[1,2,3] Onset typically occurs in younger patients in the second to fourth decade of life, and have predominantly been reported in the pediatric and juvenile patient populations.[1,2,4-7] The prevalence of HMF noted among men and women has differed, however recent studies have concluded women tend to be more affected.[3,5] HMF occurs more commonly in populations with darker skin phototypes.[1,2,4,5,7-9] The presenting hypopigmented achromic lesions closely resemble commonly seen inflammatory rashes with pigmentation loss, however the distribution and subtle uncommon features can provide clues clinically. Treatment is similar to that of vitiligo and atopic dermatitis. The prognosis tends to be excellent in these younger patients, however close follow up is necessary as recurrence rates are high.[1,2]

CASE

A 25-year-old woman presented for an evaluation of "white patches" all over her body for the past six years.

History The patient reported six years ago she had a red rash develop on her arms that then turned white, followed by additional areas on arms and legs described as having a lighter outer rim and scaly redness on the inner portion. However, she reported all the white patches have remained stable with no new lesions. Additionally, she

reported the lesions become more pronounced when out in the sun. She appeared her stated age, well-developed and well-nourished, and her past medical history was noncontributory. The patient reported having been seen by a pediatrician years ago when a biopsy was performed, given the diagnosis of vitiligo, and was subsequently told there was no treatment for her condition. She had no additional significant personal past medical or family history.

Physical examination A total body skin examination (TBSE) was performed and on examination appreciated patient to be of Fitzpatrick skin type III,[10] with ill-defined scattered splotchy hypopigmented patches with some overlying erythema and fine scale of bilateral anterior and posterior lower extremities, upper extremities, buttocks, and abdomen *(see Figures 1-3).* The patient's back, neck, face, palms, and soles were clear. A lymph node exam was not performed.

Diagnostic testing A 2 mm punch biopsy was performed on her right posterior calf and sent to an academic medical center dermatopathology lab. A complete blood cell count with differential, liver function tests, and lactate dehydrogenase were completed and found to be unremarkable. Additionally, a Sézary count was ordered to rule out the possibility of Sézary Syndrome, a rare subtype of CTCL; however the patient did not complete due to insurance coverage.

Diagnosis and outcome The differential diagnosis included vitiligo, atopic dermatitis, hypopigmented mycosis fungoides, and post-inflammatory hypopigmentation.

Formal dermatopathology demonstrated super-ficial CD8-positive lymphoid infiltrate with slight epidermotropism, CD8 immunostaining avidly labeled the infiltrate, including a tiny focus of epidermotropic cells, and the overall findings were suggestive of hypopigmented mycosis fungoides (HMF). There was no dermatopathologic evidence of vitiligo or atopic dermatitis.

Greater than 10 percent of the patient's body surface area (BSA) was involved, and when coupled with the histopathologic findings, her staging fell under the classification of stage IB, T2aN0M0. The patient received narrow band UVB phototherapy (nb-NVB) three times per week for approximately two months, then decreased to two times per week for one month. She was initially prescribed clobetasol 0.05% cream to apply to the whole body once daily; however, after 3.5 weeks, the patient reported her insurance would not

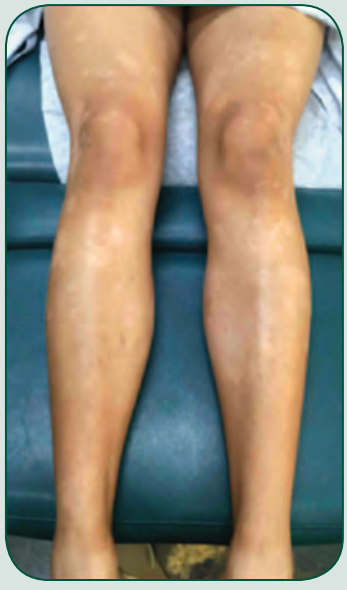

Figure 1.
Ill-defined scattered hypopigmented patches with overlying fine scale and erythema on bilateral anterior lower extremities.
Image appears courtesy of Candice E. Macari DMSc, MSPAS, MPH, PA-C

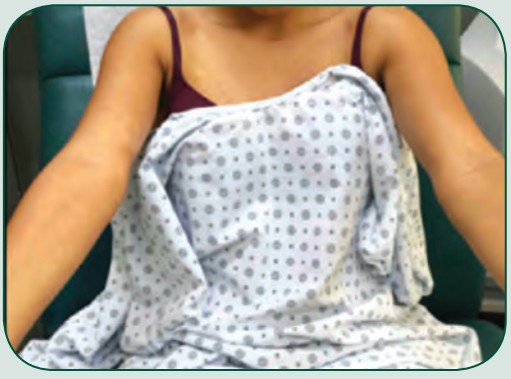

Figure 2.
Ill-defined hypopigmented patches with overlying fine scale and erythema on chest and bilateral proximal upper extremities.
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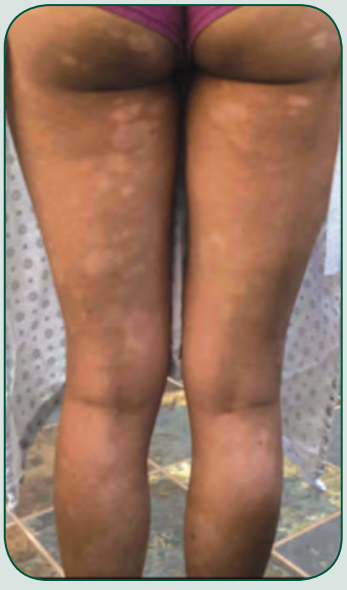

Figure 3.
Ill-defined hypopigmented patches with overlying fine scale and erythema on bilateral posterior lower extremities and buttocks.
Image appears courtesy of Candice E. Macari DMSc, MSPAS, MPH, PA-C

cover a large quantity greater than 60 grams in a single prescription, and would only fill multiple small 15-gram tubes. Patient was then prescribed betamethasone 0.1% cream to apply once daily, and then decreased to three times per week application.

One month of therapy provided significant improvement with skin re-pigmentation and almost complete resolution of erythema. She had mild sunburn-like symptoms from her nb-UVB phototherapy; otherwise, she had no notable adverse reactions.

Upon receiving the pathology report, she was referred to the closest academic medical center's cutaneous lymphoma clinic, who favored the biopsy results, and agreed with the treatment plan provided. Providers at the clinic were encouraged by the patient's significant response exemplified by re-pigmentation and decreased erythema. Additional treatment recommendations were given, including decreasing the interval of nb-UVB phototherapy from three times per week to two times per week for three months after completing another six weeks of treatment of nb-UVB at three times per week. She completed approximately 18 weeks and a total 32 sessions of nbUVB phototherapy combined with mid- to high-potency topical corticosteroids. The patient was told to follow up in the specialty clinic after completing the therapeutic plan.

Unfortunately, the patient was lost to follow up in the dermatology clinic after approximately five months from initial and subsequent visits, and final pictures of her re-pigmentation and clearance were not collected.

HYPOPIGMENTED MYCOSIS FUNGOIDES

Demographics HMF typically affects younger individuals in the second to fourth decades of life; African American, Middle Eastern, Asian, and Hispanic descent; and those of darker skin types higher on the Fitzpatrick scale skin phototypes IV-VI *(see Table 1)*.[1,2,4,5,7] HMF comprises approximately 58-91 per cent of pediatric MF cases, with the youngest reported case as young as 6 months old.[5,8] Interestingly, the disease is more predominant among younger female patients.[3,5] Overall, studies show a higher incidence of HMF among pediatric and juvenile populations.[2,4,6,7]

TABLE 1: Fitzpatrick Skin Phototype

Type I	Light, pale white
Type II	White, fair
Type III	Medium, white to olive
Type IV	Olive, moderate brown
Type V	Brown, dark brown
Type VI	Very dark brown, black

Histopathology The pathogenesis behind HMF is not completely understood, and is similar histopathologically to other variants of MF.[4,5] Research has shown HMF is characterized by the uncontrolled expansion of monoclonal malignant T-cells involving the skin, eliciting an antitumor response.[5] HMF is thought to remain in the equilibrium phase of the cancer immunoediting process contributing to HMF not progressing past stage IB.[5] On immunohistochemical findings, epidermotropism and CD8+ T-cells predominate, and their cytotoxic effect are likely the cause for the hypopigmented patches, which differs from other MF variants.[1,4,5,9,11] Additional studies show similar histopathology of skin biopsy specimens upon staining with the predominance of CD8 infiltrates, as well as CD4 infiltrates, mixed CD4/CD8, CD7 loss, atypical lymphocytes within the epidermis forming Pautrier microabscesses, and areas of decreased epidermal melanin.[3,4,5,11,12] Researchers have suggested patients presenting with a scaly erythema component correlates more with an advanced stage compared to only hypopigmented lesions on histopathology.[12]

Clinical presentation The patient will most commonly present with ill-defined hypopigmented patches or plaques, possible scaly erythema, in areas not typically associated with vitiligo.[4,5,12,13] Typically, patients are asymptomatic, without burning or pruritus of the affected areas; however, pruritus, increased skin sensitivity, skin atrophy, and some cases of peripheral lymphadenopathy have been reported.[4,5,9] The presenting lesion distribution typically occurs on non-sun-exposed areas of the skin located on the extremities, trunk, below the waistline on buttocks, and spares the face, hands, palms and soles, although facial involvement has been reported.[2,4,5,7-9,11,14] Patients rarely progress beyond stage IB, and remain in patch stage.[1,5]

Diagnostic work-up Studies differ in reported average time frame of disease onset to diagnosis ranging from 3.6 years to 5.3 years.[4,15] Differentiation clinically between similar hypopigmented inflammatory rashes and histopathologically between HMF and inflammatory vitiligo can be challenging.[8] Close attention to the location, more commonly in a bathing suit distribution, the appearance, and symptoms of the rash aid in making the diagnosis, along with skin biopsies to confirm. Pictures should be taken to record initial presentation, and at subsequent visits to document progression, stabilization, or resolution. A thorough check for lymphadenopa-

thy should be performed, although palpable nodes tend to be benign.[5,9] Clinicians may be reluctant to perform a biopsy on younger patients due to resulting undesirable cosmesis. This in turn leads to misdiagnosis and delay in treatment, resulting in possible disease persistence or stage progression.[2]

The type of biopsy is crucial for proper diagnostic workup. If a patient presents with different anatomic sites affected, then a biopsy from each of these locations could aid in definitive diagnosis.[16] A shave biopsy is ideal; however, a punch biopsy is sufficient. The shave should be broad and deep enough to include the dermoepidermal junction as the malignant infiltrate is epidermotropic.[16] The broad shave specimen provides a larger field to extract more DNA for further tests, including perform flow cytometry analysis, T-cell gene rearrangement studies, and immunohistochemical stains to determine the involvement of lymphocytes.[16,17] Special pathology testing is necessary, and depending upon a clinic's location, access to a dermatopathologist who has more experience with these specific tests may not be readily available. A clinic may need to send off their specimens to a more equipped or specialized pathology department. Further laboratory tests aid in diagnosis and exclusion of other clinical subtypes of CTCL and are at the discretion of the clinician.

Differential diagnosis The presenting cutaneous findings of HMF can be mistaken for commonly seen hypopigmented skin disorders in the dermatologic and general practice settings, and therefore the differential diagnosis can be extensive *(see Table 2).* The most common diagnosis to rule out include vitiligo, atopic dermatitis (AD), pityriasis alba (PA), tinea versicolor (TV), post-inflammatory hypopigmentation (PIH), idiopathic guttate hypomelanosis (IGH), and less common syphilis, sarcoidosis, pityriasis lichenoides chronica, and leprosy.[1,2,4,9]

TABLE 2: Hypopigmented mycosis fungoides differential diagnosis

Vitiligo
Atopic dermatitis
Pityriasis alba
Tinea versicolor
Post-inflammatory hypopigmentation
Idiopathic guttate hypomelanosis
Pityriasis lichenoides chronica
Syphilis
Sarcoidosis
Leprosy

Treatment considerations HMF treatment follows early stage classic MF treatment guidelines.[7] Treatment for these young HMF patients consist of skin-directed therapies including, but not limited to, the use of mid- to high-potency topical corticosteroids, oral psoralen with ultraviolet A phototherapy (PUVA), and nbUVB phototherapy.[1,2,4,13] Previously, PUVA tended to be the treatment of choice.[11] PUVA and nbUVB have both shown to provide up to a 90 percent response rate and remission of lesions in less than two months.[7] Recent literature suggests patients with HMF do not need systemic therapies.[5]

Currently, first-line treatment is nbUVB phototherapy over the course of a few months to a year and/or topical corticosteroids have shown to be the most successful and preferable treatment for disease control of HMF.[5,7,11,13] This closely resembles the commonly used treatments for vitiligo and atopic dermatitis. Narrow band ultraviolet B phototherapy (nbUVB) works by suppressing the proliferation of malignant T-cells.[5]

Studies utilizing localized treatment of smaller isolated lesions with 308 nm excimer laser have shown good promise with complete clearance and repigmentation after weekly treatments for one year.[11] This treatment option has the potential to be particularly advantageous over nbUVB phototherapy whereby avoiding unnecessary exposure to ultraviolet (UV) radiation of unaffected areas.[11]

Staging, prognosis, and recurrence prevention The four evolutionary phases of MF include pre-MF, patch, plaque, and then tumor. MF and the variant HMF are staged using the tumor-node-metastasis (TNM) classification system, and HMF tends to slowly progress and remain in stage I (patch stage) when treated.[4,13] In general, affected children rarely progress past stage IA or IB.[1,4,5,7,9]

The prognosis for HMF in younger patients is favorable, with an indolent course; however, recurrence rate is high, and long-term follow up is required.[5,7,13,15] The particular presence of hypopigmentation is considered to be a favorable prognostic factor.[9] Literature suggests hypopigmented lesion repigmentation and complete repigmentation correlates with an effective treatment response, and clinical and histopathologic resolution.[4] New literature supports the finding of hypopigmentation in HMF, its early onset in those younger in age, and the predominance of CD8+ T-cells, are good prognostic indicators for an active Th1/cytotoxic antitumor immune response, which correlates with HMF rarely advancing beyond stage IB.[5] The development of new

hypopigmented lesions at any given time throughout remission suggests relapse.[4]

Regular patient follow up is important in these patients as studies show recurrence is common after treatment withdrawal.[1] Retrospective studies are lacking further investigation into the potential timeline of recurrence onset following treatment discontinuation.[4] Patients who have remained in follow up for up to 10 years have not shown to have progressed to advanced stages.[2]

CONCLUSION

HMF is a rare form of CTCL most commonly occurring in younger patients at an earlier stage, in darker skin types, and presenting cutaneous findings can mimic other common hypopigmented skin disorders in the dermatologic and general practice settings. This can lead to misdiagnosis and delay in treatment. Therefore, HMF should be on the differential diagnosis of clinicians when a patient presents with hypopigmented patches. Treatment for these young patients with HMF consist of phototherapy and/or topical corticosteroids. Repigmentation of the hypopigmented lesions correlates with successful treatment on a clinical and histopathologic level, and new hypopigmented lesions during remission suggest relapse. The majority of HMF patients remain in stage I, and prognosis is favorable, although recurrence rate is high, and close follow up is recommended.

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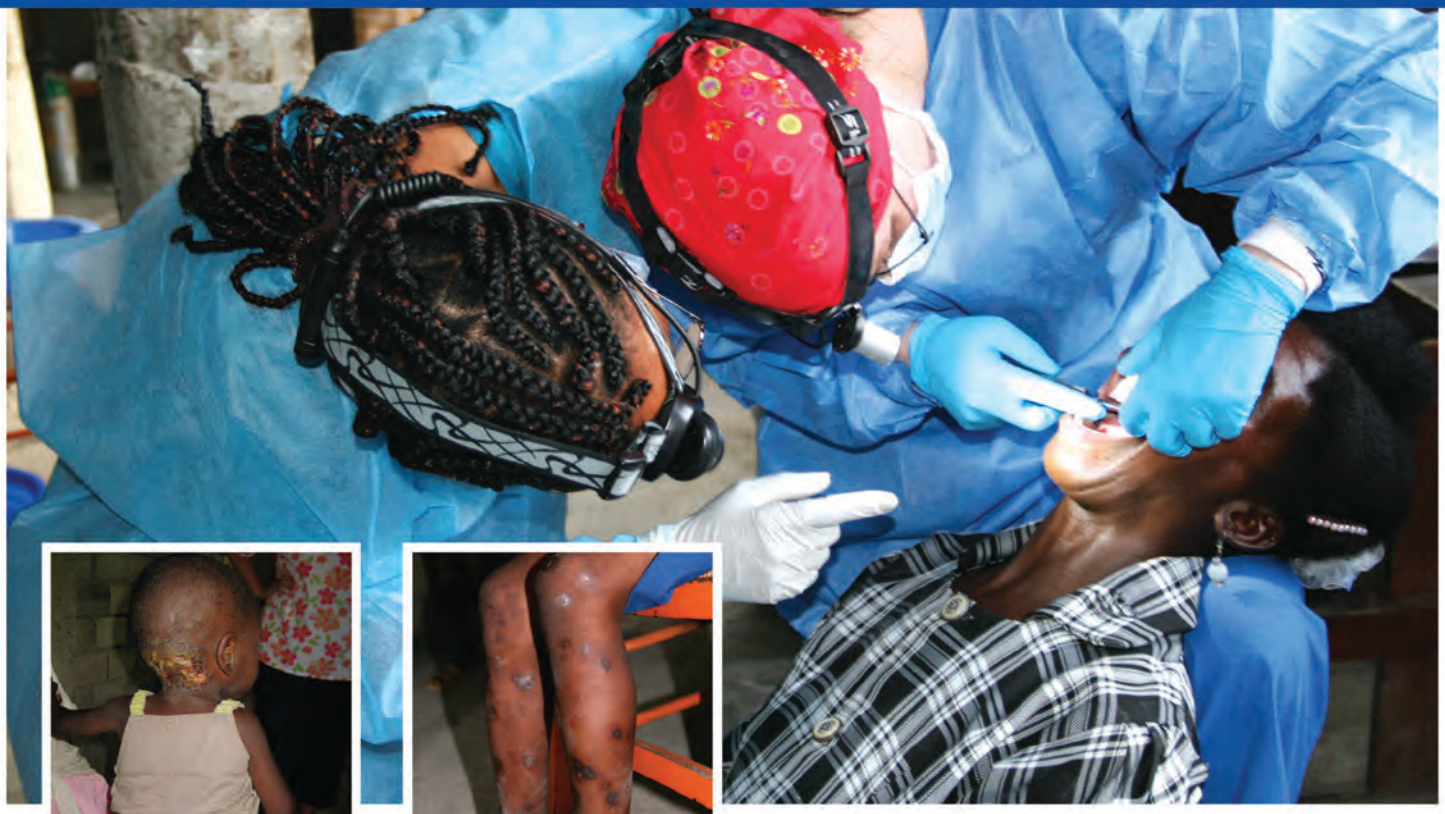
Candice E. Macari, DMSc, MSPAS, MPH, PA-C; *is from Marin Health Breast Surgical Oncology & Gynecologic Surgery in Greenbrae, California.*

Disclosure: *The author has disclosed no potential conflicts of interest, financial or otherwise, relating to the content of this article.*

Address for Correspondence: *Candice E. Macari, DMSc, MSPAS, MPH, PA-C; e-mail: candice.macari@gmail.com*

DPAF Medical Mission Academy



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Evaluating the Use of Supplemental Training Technologies in Dermatology Education

By Mallory M. Aycock, MPA, PA-C; Craig D. Marker, PhD; and Philip J. Kellman, PhD

The Journal of Dermatology Physician Assistants is proud to present "Evaluating the Use of Supplemental Training Technologies in Dermatology Education" by Mallory M. Aycock, MPA, PA-C; Craig D. Marker, PhD; and Philip J. Kellman, PhD. Although it focuses on areas outside the scope of the practicing dermatology PA, the original research discussed within explores education methods that have potential to improve PA knowledge of dermatology concepts and is therefore likely of high interest to our readership.

ABSTRACT

Physician assistants (PAs) are licensed to evaluate, diagnose, and treat dermatologic conditions. Data show that medical students have less than optimal dermatology diagnostic abilities. Although no known data exists for PA students, similar medical school and PA school training methods highlight a need for improved dermatology education in medical and PA programs. This project explored the use of perceptual and adaptive learning modules (PALMs) that target pattern recognition skills with PA students to hopefully improve PA knowledge of dermatology concepts.

KEYWORDS

Dermatology, physician assistant education, training technologies, perceptual and adaptive learning modules, PALMs

BACKGROUND

There are no known studies on dermatology training in PA programs. The data on medical school training suggest that about 50 percent of medical schools in the United States provide 10 or less hours of dermatology training, while about eight percent require no instruction in dermatology.[1,2] One study by Ulman et al demonstrates medical students are not proficient in diagnosis and treatment of dermatologic disease despite about 18 hours of training, and the authors of this study suggest evaluation of dermatology curriculum nationwide.[1] While our PA program provides roughly 29 hours of didactic education in dermatology, mastery of dermatology concepts cannot be achieved without practice.[3] There is a discrepancy between learned knowledge in medical education and application of that knowledge during clinical practice, notably in medical skills that require recognition of clinical patterns, such as dermatology.[3] Traditional teaching methods are thought to lack in the training of perceptual learning, defined as "experience-induced changes in the way perceivers extract information."[4] Whereas most instruction emphasizes explicit declarative and procedural learning, other crucial components of expertise, including pattern recognition, fluency, and clinical intuition involve different learning systems and advance through more implicit and interactive learning experiences.[3,4] Diagnostic expertise in medical learners advances through classification episodes that incorporate a range of instances that encompass normal and pathological variations across relevant categories. In traditional medical education in dermatology, as in other domains, these aspects of learning occur somewhat unsystematically through recurrent clinical experiences or exposures to patients with dermatology complaints.[5,6] Gaining this experience may take large amounts of time that is not afforded in conventional didactic dermatology education models.[2]

One resource proven to bridge this gap in medical education is an online supplemental technology resource developed by Insight Learning Technology, Inc. called Perceptual and Adaptive Learning Modules (PALMs).[3,7] PALMs were created as a technology resource to help students increase mastery of medical skills through pattern recognition. They are intended to supplement didactic training by providing practice examples that enable optimization of rate and retention of performance in specific medical skill areas.[3,7] PALMs have provided significant improvement in medical school education and medical resident training in the areas of echocardiogram interpretation, histopathology, electrocardiogram interpretation, and dermatology.[3,6,8,9] This supplemental platform, however, has never been studied in dermatology training specifically in PA education.

PALMs target perceptual learning—changes in the pickup of information that occur in a given domain as a result of practice or experience.[4] They incorporate

a number of principles of learning, including spacing and interleaving, and systematic variation of exemplars, to accelerate expert pattern recognition skills. The adaptive components of PALMs pair advanced adaptive algorithms with perceptual learning, such that the spacing and recurrence of each learning category is based on each learner's accuracy and speed with exemplars of that category in ways that tend to optimize the efficiency and durability of learning. The adaptive elements in PALMs also track learning of each category to mastery criteria that include both accuracy and fluency.[3,10] Currently, there are five dermatology PALMS allowing students to practice lesion morphology, lesion distribution, lesion configuration, lesion identification (skin cancer), and lesion diagnosis (**Figure 1**). In four out of five dermatology PALMs, students are presented with an image that requires them to choose a diagnosis or description (**Figure 2, left**). The exception is the "Lesion Identification: Skin Cancer" PALM, where the user is presented with two images, a regular image and a dermoscopic image, and the software then requires them to choose a diagnosis using both pictures (**Figure 2, right**). For all modules, after the student selects an answer choice, the software displays the correct response. The PALMs software adapts to the student user by adjusting presented cases based on the learner's performance, thus making it more customized for each individual student learner. This adaption also allows the student to improve on areas of weak understanding and improve proficiency of the dermatology concepts listed in **Figure 1**.[3,6,8,9] This supplemental platform, however, has never been studied in dermatology training, specifically in PA education. Therefore, the aim of this project was to evaluate the use of PALMs in PA education.

RESEARCH QUESTIONS

1. Will use of supplemental training technologies in dermatology education improve PA student knowledge and diagnostic accuracy of dermatologic conditions?

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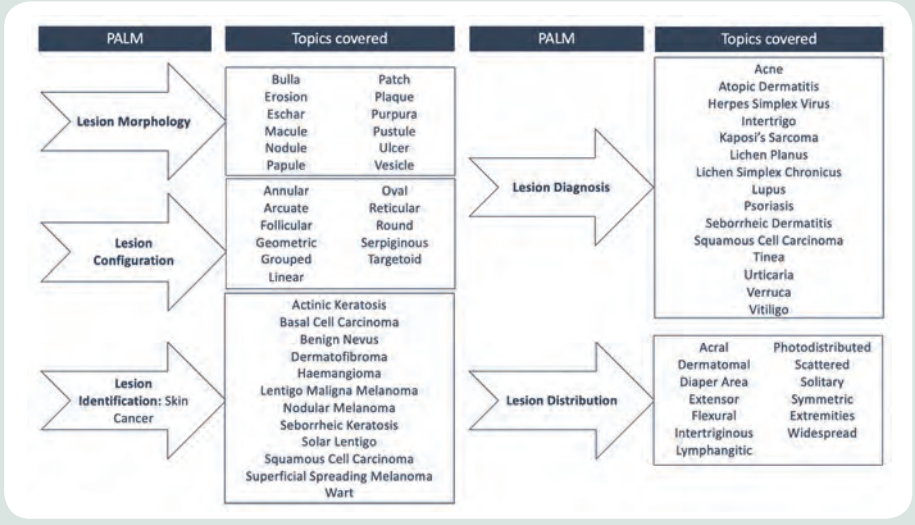

Figure 1.
Dermatology PALMs and Topics Covered in Each PALM (https://med.insightlt.com/site/, Insight Learning Technology, Inc. ©2021)

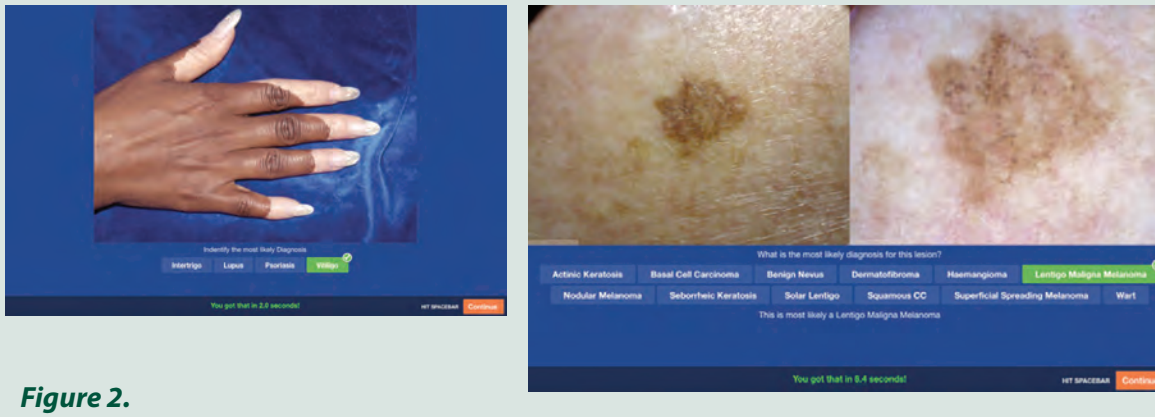

Figure 2.
(left) Example of "Lesion Diagnosis" PALM (right) Example of "Lesion Identification: Skin Cancer" PALM with one regular and one dermoscopic image (images: https://med.insightlt.com/site/, Insight Learning Technology, Inc. ©2021)

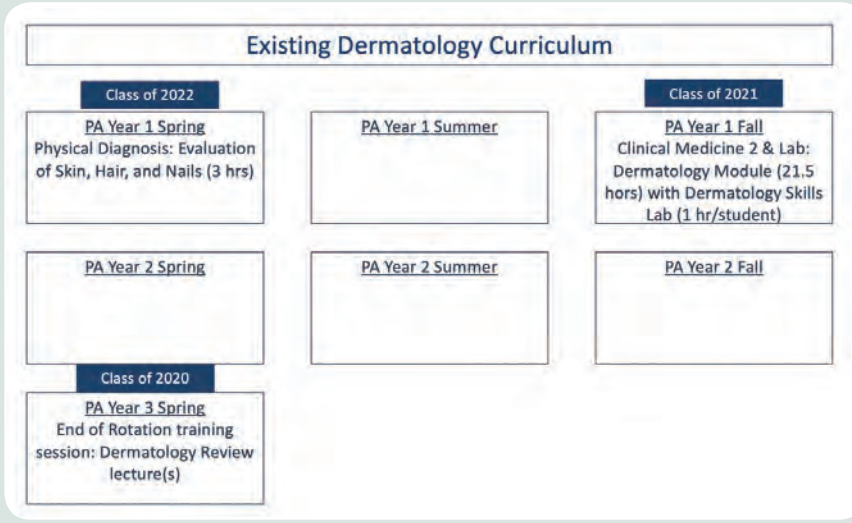

Figure 3.
Current dermatology curriculum in our PA program (white boxes) and stage of education for Classes of 2020, 2021, and 2022 at the time of the educational intervention (navy boxes)

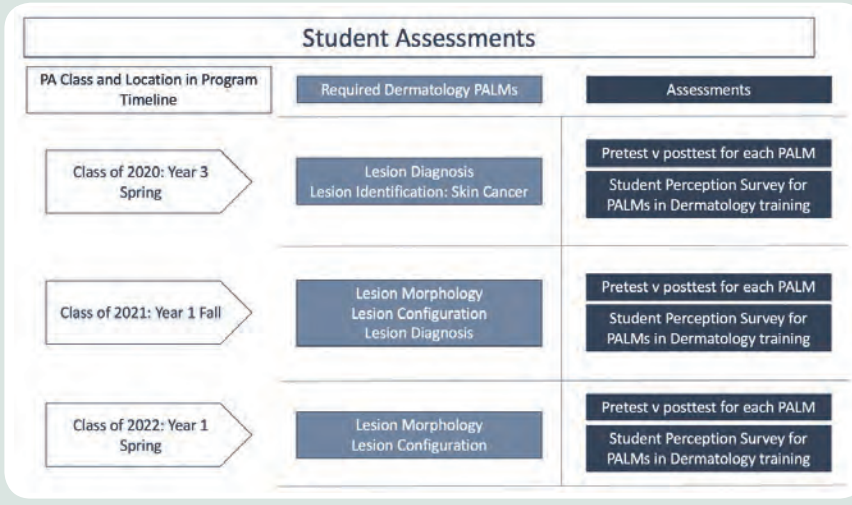

Figure 4.
Required dermatology PALMs and PA student assessments by cohort

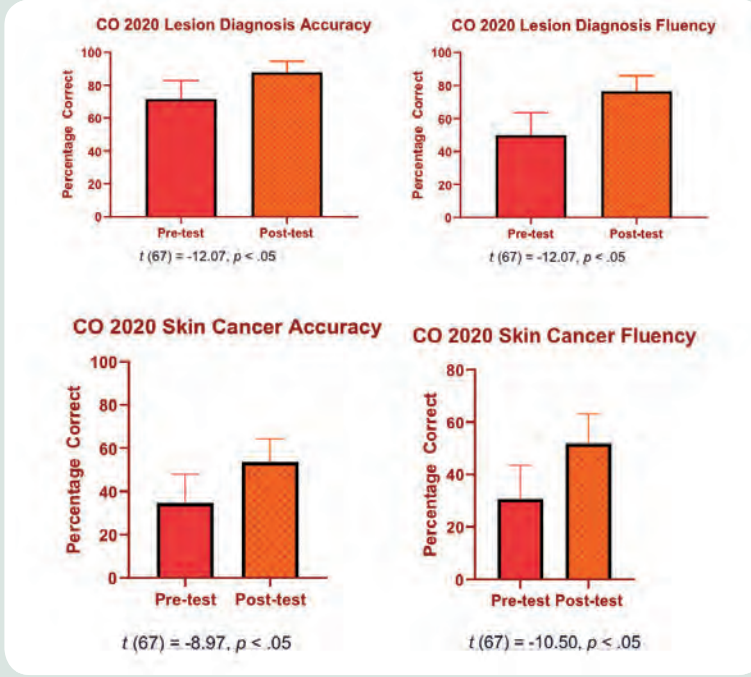

Figure 5.
Class of (CO) 2020 student performance results by PALM online module

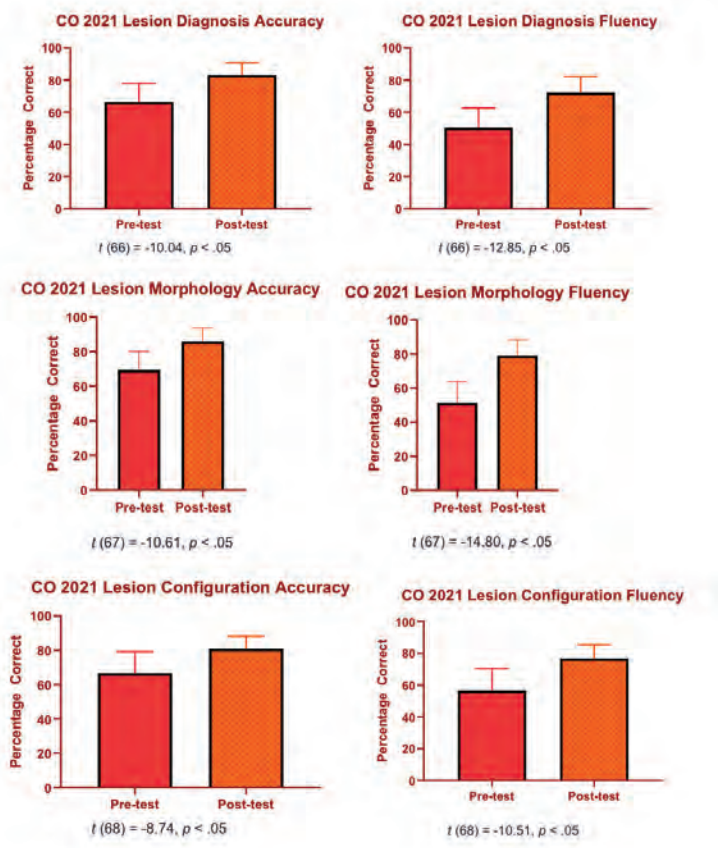

Figure 6.
Class of (CO) 2021 student performance results by PALM online module

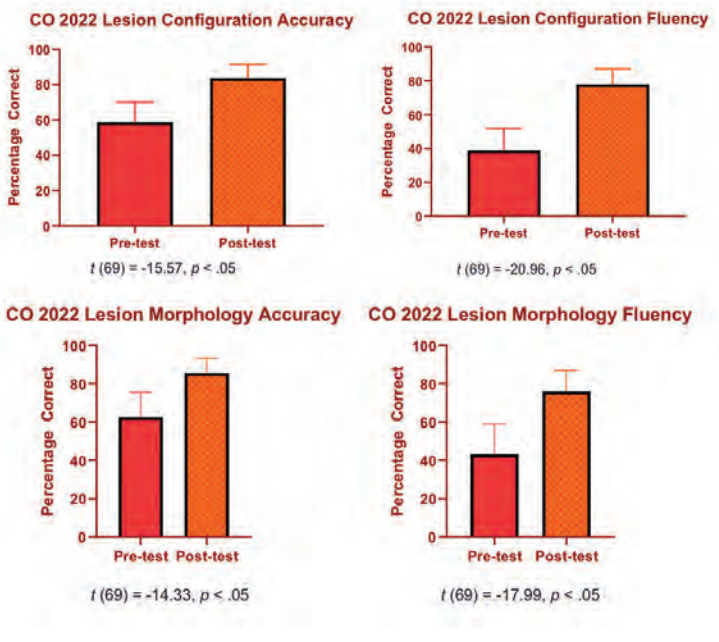

Figure 7.
Class of (CO) 2022 student performance results by PALM online module

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2. Will use of supplemental training technologies in dermatology education improve PA student perceptions of their dermatology knowledge and skill on clinical rotations?

RESEARCH METHODS

Group and Sample Size

This study was completed at a PA program from a single university. All students from the Class of 2020 (68 students), Class of 2021 (69 students), and Class of 2022 (70 students) used the PALMs educational intervention during the study period, though each class was in a different stage of their education (**Figure 3**).

Methods

Students are typically trained in dermatology at different times in the curriculum (**Figure 3**). The traditional lecture-based and lab-based education was maintained in this study, totaling almost 29 hours of instruction. This instruction includes training in Physical Diagnosis of Skin, Hair, and Nails (3 hours) along with a Clinical Medicine Dermatology module (21.5 hours) covering dermatologic disease states. Students also participate in a hands-on skills lab where they practice excisions, punch biopsies, shave biopsies, and dermoscopy. Lastly, all students attend dermatology review lectures during their clinical education year at an "End of Rotation" (EOR) training session (**Figure 3**).

For the educational intervention, each cohort was required to complete dermatology PALMs specific to their level of education within 2 to 4 weeks of completing their lecture series or lecture-based module (**Figure 4**). For each dermatology PALM, the technology platform was set. Students completed a pretest, the PALMs training module, then a posttest. Students were then asked to voluntarily complete a survey regarding their experiences using PALMs in dermatology training.

Data Collection and Statistical Analysis

Institutional Review Board (IRB) approval was obtained. IBM SPSS statistical software was used for all analyses. Perception survey responses and dermatology PALMs pretest and posttest scores were collected (**Figure 4**). Data were de-identified and aggregated by the following groups: Class of 2020, Class of 2021, and Class of 2022. Paired-sample t-tests were used to compare pretest and posttest scores for each group to look for changes before and after dermatology PALMs use, specifically looking at accuracy (percentage of images correctly identified) and fluency (percentage of images correctly interpreted within a response time of 15 seconds or less). Statistical significance was set at $p<0.05$.

In addition to evaluating PA student knowledge, we assessed PA student perceptions of PALMs using a 5-point Likert scale perception survey. Responses ranged from "strongly disagree" to "strongly agree." For the purposes of this project, responses of "agree" and "strongly agree" were combined and noted as "respondents in agreement." Overall survey response rates for Classes 2020, 2021, and 2022, were 59.94, 92.75, and 88.57 percent, respectively.

RESULTS

Student Performance

Class of 2020

The Class of 2020 was in their seventh semester of PA education at the time of the study ("PA Year 3 Spring," **Figure 3**). This cohort was required to complete the "Lesion Diagnosis" and "Lesion Identification: Skin Cancer" modules. Students performed an average of 195 and 291 practice cases, respectively, for each module and it took students an average of 21.9 minutes and 44.2 minutes, respectively, to complete each module. For both the "Lesion Diagnosis" and "Lesion Identification: Skin Cancer" modules, there was statistically significant improvement ($p<0.05$) of pretest to posttest scores for both accuracy and fluency (**Figure 5**).

Class of 2021

The Class of 2021 was in their third semester of PA education at the time of the study ("PA Year 1 Fall," Figure 3). This cohort was required to complete the "Lesion Morphology," "Lesion Configuration," and "Lesion Diagnosis" modules. Students performed an average of 102, 75, and 202 practice cases, respectively, for each module and it took students an average of 11.9 minutes, 8.9 minutes, and 26.6 minutes, respectively, to complete each module. For the "Lesion Morphology," "Lesion Configuration," and "Lesion Diagnosis" modules, there was statistically significant improvement ($p<0.05$) of pretest to posttest scores for both accuracy and fluency (**Figure 6**).

Class of 2022

The Class of 2022 was in their first semester of PA education at the time of the study ("PA Year 1 Spring," **Figure 3**). This cohort was required to complete the "Lesion Morphology" and "Lesion Configuration" modules. Students performed an average of 105 and 85 practice cases, respectively, for each module; it took students an average of 11.5 minutes and 11.1 minutes, respectively, to complete each module. For both the "Lesion Morphology" and "Lesion Configuration" modules, there was statistically significant improvement ($p<0.05$) of pretest to posttest scores for both accuracy and fluency (**Figure 7**).

Student Perceptions

More than 80% of respondents from all three cohorts agreed that utilizing the PALMs improved their

overall understanding of dermatology. More than 60 percent of respondents from all three cohorts agreed that utilizing PALMs improved their ability to interpret skin lesions and their accuracy in diagnosing dermatology conditions. Lastly, more than 70 percent of respondents from all three cohorts agreed that "online dermatology modules (PALMs) should be added to the curriculum of medical education programs for PAs." (**Table 1**)

DISCUSSION

***Research Question #1:** Will use of supplemental training technologies in dermatology education improve PA student knowledge and diagnostic accuracy of dermatology concepts?*

For all three cohorts, the use of supplemental PALMs improved student knowledge in dermatology conditions and diagnoses. These findings suggest that PALMs supplemental modules are a method to provide students with multiple practice examples that enable students to improve their knowledge base in dermatology. Because PALMs are housed in online modules, this supplemental training is an efficient way for students to practice concepts before seeing patients. This PA student performance improvement aligns with research using PALMs for training of medical students and medical residents.[6,8,9]

The gains seen in these data came from relatively brief learning interventions. With the mastery criteria used in the PALMs tested here, completion times averaged under 20 minutes, with some being completed in an average of about 11 minutes. These results are consistent with earlier work in indicating that PALMs

PALMs Student Perception Survey	% of Student Respondents in Agreement (CO2020)	% of Student Respondents in Agreement (CO2021)	% of Student Respondents in Agreement (CO2022)
I feel the online dermatology modules (PALMs) improved my overall understanding of dermatology.	80.55%	85.94%	96.78%
I feel the online dermatology modules (PALMs) helped me to correctly identify abnormal skin lesions.	72.23%	79.36%	--*
I feel the online dermatology modules (PALMs) helped me improve my ability to interpret skin lesions.	69.45%	76.19%	93.55%
I feel the online dermatology modules (PALMs) helped me improve the rate at which I can interpret skin lesions.	58.33%	78.13%	85.48%
I feel the online dermatology modules (PALMs) will improve my ability to care for patients with dermatologic complaints.	55.56%	64.07%	80.32%
I feel the online dermatology modules (PALMs) will improve my accuracy in diagnosing dermatologic conditions.	61.11%	67.19%	75.81%
I feel the online dermatology modules (PALMs) have improved my confidence in assessing skin conditions.	48.57%	64.06%	77.42%
I feel online dermatology modules (PALMs) should be added to the curriculum of medical education programs for Physician Assistants.	72.22%	81.25%	96.77%

Table 1.

PA Student perception survey results; respondents in agreement per cohort (Classes of (CO) 2020, 2021, and 2022)

**This question was not asked of the Class of 2022 since it was not applicable to the PALMs they completed.*

address missing components of learning, such as pattern recognition, that are not much advanced by traditional instructional methods.[3,6-9] Traditional learning methods in medical education (e.g., lectures and textbook) allow students to study and learn but often lack opportunity to practice the concepts. With PALMs, students are actively practicing the material they are learning (e.g., diagnosing skin lesions). PALMs systematic interventions targeting perceptual learning can begin to exert their effects in a short time, given appropriate use of the software. Lastly, the pretest levels did not vary greatly by cohort. This result indicates that PALMs have a role in addressing aspects of learning that might not be covered by conventional instruction.

Research Question #2: Will use of supplemental training technologies in dermatology education improve PA student perceptions of their dermatology knowledge and skill on clinical rotations?

Results of the perception surveys note overwhelmingly positive feedback from use of dermatology PALMs in all three cohorts for all questions asked (**Table 1**). It is important to highlight that respondents agreed that use of dermatology PALMs improved their overall understanding of dermatology, improved their ability to interpret skin lesions, and improved their ability to diagnose dermatology. These results support that dermatology PALMs improved PA student perceptions of their dermatology knowledge and skills. Lastly, a majority of student respondents from all three cohorts felt these dermatology PALMs should be added to PA curriculum, which captures an overall level of satisfaction with the modules and emphasizes student willingness to continue using these modules in PA education.

Instructor Implementation Perspective

Combining e-learning modules with traditional medical education methods has been shown to produce a more time-efficient and effective learning system than traditional learning methods alone.[11] As dermatology educators, this supplemental online training platform was simple to implement into our PA program curriculum. The average completion time for each module was about 19 minutes (range: 8-44 minutes), which made adding these modules achievable in a challenging and full curriculum. The adaptive nature of these modules allow individualized learning for all students and real-time feedback as they practiced, which was noted to be helpful for all students no matter their areas of strengths or weaknesses.

It should also be highlighted that these modules have images of patients with all six Fitzpatrick skin phototypes, allowing students to practice dermatology concepts on patients with variable skin pigmentation. Although we observed benefits of perceptual learning with PALMs ability to address aspects of learning that are often difficult to address with traditional instruction, we do not feel these interventions replace the important aspects of conventional instruction used in dermatology education. In fact, the synergy of PALMs as additions to learning with more conventional elements may be particularly powerful in their long-term consequences for medical practice.

Limitations and Future Research

The dermatology PALMs modules were not inclusive of every dermatology lesion or abnormality students may encounter, therefore limiting students' ability to practice all types of dermatology cases. The findings presented here might not be generalizable since this was a single-site study; conducting this research at multiple PA programs would improve the validity. Future research should be considered to note the impact of dermatology PALMs on Physician Assistant National Certifying Examination (PANCE) board performance and/or clinical rotation performance. It would also be beneficial to study the use of dermatology PALMs in practicing PAs.

CONCLUSION

The combination of improved student performance data and positive student perception study data supports the continued use of dermatology PALMs in the dermatology training of PA students at our PA program.

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Acknowledgements: *This project was funded by the Dermatology PA Foundation (DPAF) Physician Assistant Research Grant Program. We would like to acknowledge and show appreciation to the Society of Dermatology Physician Assistants (SDPA), DPAF, and Sun Pharmaceuticals for supporting this project through the 2019 DPAF Physician Assistant Research Grant Award. We also gratefully acknowledge support from NIH/NCI R01CA236791*

Mallory M. Aycock, MPA, PA-C *served as the Principal Investigator on this grant project. She is a graduate of Medical College of Georgia in Augusta, GA. She has practiced both in Dermatology and Surgery. Mallory is currently an Adjunct Clinical Assistant Professor at Mercer University in the Department of Physician Assistant Studies.*

Craig D. Marker, PhD *served as the Statistician on this grant project. He received his PhD and MS in clinical psychology from Rosalind Franklin University and a postdoctoral respecialization in quantitative methods from the University of Virginia. Dr. Marker is Professor, Chair, and Program Director of Clinical Psychology at Mercer University.*

Philip J. Kellman, PhD *did not participate in the grant project. He contributed to the manuscript in the area of perceptual and adaptive learning, as this is his area of expertise. Dr. Kellman received his PhD from the University of Pennsylvania. He is Distinguished Professor of Psychology, Adjunct Professor of Surgery, and the current Cognitive Area Chair in the Department of Psychology at the University of California, Los Angeles.*

Disclosure: *Mallory M. Aycock, MPA, PA-C, and Craig D. Marker, PhD, have disclosed no potential conflicts of interest, financial or otherwise, relating to the content of this article. Philip J. Kellman, PhD, wishes to disclose he is the author of patents in perceptual learning and adaptive learning and the founder of Insight Learning Technology, Inc., which develops learning technology to accelerate pattern recognition and expertise in medical learning and other domains.*

Address for Correspondence:
Mallory M. Aycock, MPA, PA-C
Email address: aycock_mm@mercer.edu

Contact Dermatitis in Children: Indications for Pediatric Patch Testing

By Kara Mudd, MSPAS, PA-C

ABSTRACT

Allergic contact dermatitis (ACD) is often underdiagnosed in pediatric patients, especially those with a diagnosis of atopic dermatitis (AD). Recent literature has shown that the incidence of ACD in children is increasing and several factors of atopy play a role. It is important to recognize the possibility of ACD in the pediatric population and perform extended patch testing with the North American Contact Dermatitis Group (NACDG) core series in these patients. Patch testing can help with allergen identification and management of chronic dermatitis.

KEYWORDS

Allergic contact dermatitis, atopic dermatitis, pediatric allergens, pediatric patch testing

INTRODUCTION

Allergic contact dermatitis (ACD) is often under diagnosed in pediatric patients, especially those with a diagnosis of atopic dermatitis. Over the past decade the pathophysiology and treatment of chronic eczematous skin dermatitis, specifically atopic dermatitis, has led to better identification of allergic contact dermatitis in the pediatric population.[1]

INCIDENCE OF ALLERGIC CONTACT DERMATITIS IN CHILDREN WITH ATOPY

Allergic contact dermatitis (ACD) was once thought to be a disease primarily of adulthood, while atopic dermatitis (AD) was thought to be the predominant dermatitis of infancy and childhood. Over the past decade, ACD has been identified as a common skin condition in children ages 5-17, especially in those with a diagnosis of atopic dermatitis.[1] A recent literature review of patients age 1-18 with a diagnosis of AD revealed that between 30.5%-92.6% of patients had positive patch test results that were clinically relevant.[2] Hand eczema in children has also been reported to have a high probability of ACD.[3] ACD has been reported in children of all ages, including neonates and adolescents, and the incidence is thought to be increasing.[4]

PATHOPHYSIOLOGY OF ACD

The pathogenesis of ACD is a Type IV delayed hypersensitivity reaction. It begins with the sensitization phase when the patient is initially exposed to the allergen. Antigen-presenting cells then present the allergen to T lymphocytes. Upon repeat exposure to the allergen, the memory T lymphocytes activate the inflammatory cascade within 12 to 24 hours of exposure and result in a localized or systemic dermatitis.[5] It is important to note that the skin or systemic symptoms may begin days, or sometimes weeks, after the exposure. It is deemed that several factors increase the lifetime risk of developing ACD in pediatric patients. These risk factors include early exposure to potential allergens in topical emollients and sunscreens, play products, such as paints and slimes, and use of makeup and personal hygiene products.[6] ACD has recently been shown to be amplified in patients with both skin and respiratory atopy.[7,8] Risk is increased due to dysfunctional skin barrier and disruption of the skin microbiome that is typically seen in AD, thus allowing increased allergen penetration and activation of the inflammatory cascade.[8] An overlap of increased specific T helper cells and filaggrin mutations has also been found in both AD and ACD.[8,9]

COMMON ALLERGENS

The most prevalent contact allergens are similar between adult and pediatric patients. Exact incidence varies between studies. The most common allergens are nickel, fragrance mix, cobalt, propylene glycol, methylisothiazolinone/methylchloroisothiazolinone (MI/MCI), and formaldehyde.[10,11] In a recent retrospective cohort study of pediatric patch tests, cocamidopropyl betaine and benzoyl peroxide were included in the list of top 10 allergens.[10] It is important to note that three of the allergens mentioned above, cocamidopropyl betaine, propylene glycol, and benzoyl peroxide, are not found on the Thin-Layer Rapid Use Epicutaneous (TRUE) patch test.

Nickel and cobalt are frequently found in children's jewelry and common metallic household items, such as scissors, keys, and electronic devices. Many products marketed as "gentle" or "sensitive" for babies, the common being soaps, shampoos, moisturizers, and sunscreen may contain several other common allergens and can cause generalized or widespread dermatitis ***(Table 1)***.[4,5] It is also important to consider transfer of allergens from caregivers and siblings, especially with fragrance, isothiazolinone, and formaldehyde, when counseling on allergen avoidance. There is also the potential for allergens, such as nickel, in dietary sources and patients may benefit from diets that limit oral exposure to allergens. Benzoyl peroxide can also be a common irritant[5] that should be considered in adolescents using topical acne medications.

WHEN TO PATCH TEST

Sensitization to allergens may begin in infancy and can lead to ACD in younger children.[6] If patients have refractory dermatitis despite traditional treatment, patch testing should be considered prior to initiation of systemic

therapy.[8] Patch testing should also be considered in children with atypical dermatitis patterns, chronic hand or foot dermatitis, and adolescent onset AD.[3,6,8] Persistent dermatitis of the eyelids, genitals, or peri oral region should also increase suspicion of ACD.[6,8] See ***Table 2*** for indications for patch testing in pediatric patients.

CONCLUSION

With further research in the fields of both ACD and AD will lead to a better understanding of the role of skin barrier and genetic susceptibility to these conditions. It is important to recognize ACD in pediatric patients and offer extended series patch testing with the North American Contact Dermatitis Group (NACDG) series when possible, as common allergens can be missed on the Thin-Layer Rapid Use Epicutaneous (TRUE) test. Allergen avoidance may sometimes seem overwhelming to caregivers and patients; therefore, appropriate education on care of skin barrier and continued management of AD, in addition to allergen avoidance, is key to successful management of disease.

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Kara Mudd, MSPAS, PA-C, *is a diplomate fellow of the Society of Dermatology Physician Assistants who practices at Associates In Dermatology in Louisville, Kentucky. She has a clinical focus in Allergic Contact Dermatitis and Atopic Dermatitis. Kara is also actively involved in PA education as an Assistant Professor at Sullivan University and is currently pursuing her Doctor of Medical Science through the University of Lynchburg.*

Disclosures: *Ms. Mudd is a consultant for Regeneron Pharmaceuticals, Inc.*

Address for correspondence: *Kara Mudd, MSPAS, PA-C; email: kmuddpa@gmail.com*

TABLE 1

Common Pediatric Allergens	Common Sources (5)	Common Anatomical Locations (5)
Nickel	Metal objects, jewelry, cosmetics, foods	Hands, face, neck, trunk/ extremities/ anogenital (consider dietary sources)
Fragrance Mix	Personal care products, household cleaners, laundry detergents, cosmetics, sunscreens, essential oils	Diaper area, cheeks, face, peri-oral, neck (consider transfer from caregivers)
Cobalt	Metal objects, jewelry, tattoos, paints, cosmetics, clay, leather	Hands, face
Propylene glycol	Topical medications, oral care, household cleaners, sunscreens, personal care products	Hands, face, trunk, extremities, areas of topical medication application
MI/MCI	Personal care products, paints, laundry detergent, cosmetics	Hands, trunk, extremities
Formaldehyde	Cosmetics, textiles, personal care products, household products	Hands, trunk, extremities
Cocamidopropyl betaine	Personal care products, topical medications, cosmetics, oral care	Hands, face, peri-oral, trunk, extremities
Benzoyl peroxide	Acne medications, bleached flour, adhesives, bone cement	Face, hands, trunk

TABLE 2

Indications for Patch Testing in Pediatric Patients

- Refractory dermatitis despite traditional treatment
- Prior to initiation of systemic therapy
- Atypical patterns of dermatitis
- Adolescent onset atopic dermatitis
- Chronic dermatitis of the hands, feet, genitals, or face

Patients Report the Hidden Costs of Living with Atopic Dermatitis

By Steve Nelson

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

ABSTRACT

More than 31 million Americans live with eczema, but until recently we did not know how much money people were paying out of pocket (OOP) to manage their disease. The National Eczema Association (NEA) administered a research survey to its community of patients and caregivers to learn more about the financial burden of OOP expenses related to atopic dermatitis (AD). Prior to this study, there was no comprehensive analysis on the OOP financial burdens of AD in the United States, nor any research that investigated the impact of these OOP costs from the perspectives of patients and caregivers. Results from this effort demonstrated a significant correlation between OOP expenses and the severity of AD: patients with higher OOP costs reported more severe eczema symptoms, more days flaring per month, and more monthly visits to their healthcare provider. The study also revealed associations between higher OOP costs and the presence of comorbid conditions such as food allergies, asthma, rhinitis, anxiety, and depression. These data highlight the importance of working with patients in developing treatment plans that minimize financial burden while striving for desired care outcomes.

KEYWORDS

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

INTRODUCTION

More than 31 million Americans live with eczema, but until recently there was little known about the nature and amount of out of pocket (OOP) expenses patients incur to manage their disease. New research conducted by the National Eczema Association (NEA) has established an association between increased severity of atopic dermatitis (AD) and a corresponding increase in OOP costs for care and treatment. Symptoms and triggers of AD vary greatly across the patient community, as can the breadth of management approaches. Given the heterogeneous nature of AD, healthcare providers can benefit from a deeper appreciation of the breadth and impact of OOP costs many patients experience while managing their disease; this knowledge can empower providers and patients to collaborate on treatment plans that are effective and financially sustainable.

> *"My baby brother has to wear 100% organic cotton to avoid flaring. He flares when he touches car seats, stroller seats, really anything. No matter the weather, he has to wear clothes that cover almost every inch of his body to avoid flaring, and since his clothing has to be right for him, that gets really expensive over time."*
>
> *- Amberley Sanden on expenses related to providing care for her 18-month-old brother, who also lives with moderate-to-severe eczema.*

As the largest patient advocacy organization serving people with eczema and their caregivers, NEA conducts patient-centered real-world research and shares significant findings to increase knowledge and enable shared decision making between healthcare providers and patients. From November to December 2019, NEA researchers administered a 25-question survey to 113,502 individuals and family members living with AD. Of the 1,447 people who agreed to participate in the research survey, 1,118 individuals living with AD met the inclusion

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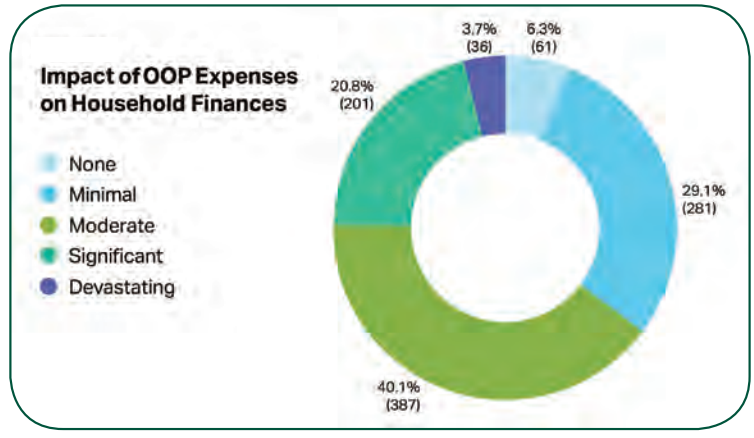
criteria for the study. Respondents provided data about the severity of their AD, frequency of flares, number of health care provider visits and out-of-pocket (OOP) costs related to the treatment of their condition; patients and caregivers also provided demographic information about themselves, including race/ethnicity, gender, household income, insurance coverage, and geographic setting.

THE BREADTH OF ECZEMA OUT-OF-POCKET COSTS

To better understand the multifaceted costs of treating AD, NEA researchers organized 22 different OOP expenses into three main categories: healthcare provider visits and prescriptions (including co-pays); non-prescription health-related products like moisturizers, sleep aids, hygiene products and dietary supplements; and complementary care items like clothing, bedding, cleaning products, and supplemental therapies like acupuncture and traditional Chinese medicine.

Each category of OOP expense had some degree of reporting by respondents reflecting the variable management nature of the disease, though some data trends did emerge. For instance, 68.7 percent of survey respondents indicated that they had incurred OOP costs for co-pays and deductibles in the past 30 days; 64.3 percent of respondents also reported that they had OOP co-pays for prescriptions covered by their insurance; and nearly half (48.6%) of the respondents spent money OOP on prescription medications not covered by their insurance. Nearly all patients in the survey reported OOP expenses for nonprescription moisturizers (94.3%).[1] Around half of the respondents had spent up to $50 in the past month on over-the-counter corticosteroids (53.5%), allergy medications (56%), and hygiene products like soap and bath water-additives (57.2%).[1]

Figure 1. *Detailed analysis of patient-reported out-of-pocket costs related to atopic dermatitis*



Some forms of eczema management were less widely reported: approximately one in five respondents (19%) had OOP expenses related to alternative treatments (such as naturopathic or traditional Chinese medicine) and 150 people (15.9%) reported OOP expenses on adjunctive therapies such as yoga or acupuncture.[2]

The research responses also underscored the wide range of total OOP costs that people with AD experience. The median annual OOP expense related to AD was approximately $600, whereas 42 percent of patients reported spending more than $1000 per year, and 8.5 percent reported more than $5,000 annually in estimated OOP expenses.[1]

INCREASED DISEASE SEVERITY, INCREASED FINANCIAL BURDEN

NEA researchers also established a significant correlation between increased severity of AD and increased OOP expenses: the worse the disease, according to patients, the more money people spent OOP trying to control it. People with higher OOP expenses were more likely to have increased AD severity, poorer control of their AD, more days actively flaring, and more monthly visits to their healthcare provider. People and caregivers with AD who spent more than $100 monthly OOP to treat their eczema were also more likely to report minimal disease control (41.1%), reliance on multiple prescription treatments (39.7%), and the use of step-up therapies such as injectable and oral medications or phototherapy.[2] Nearly 40 percent of respondents also indicated that they had spent more than 11 days actively flaring in the preceding month, whereas the number of people flaring more than 11 days in the past month jumped to 51.1 percent of respondents who spent more than $1,000 OOP annually *(Figure 1)*.[2]

Patient-reported data also indicated a significant association between increased OOP expenses and comorbid conditions such as asthma, allergic rhinitis, anxiety, and depression.[2] Over one-third of patients (36.5%) reported additional diagnoses of anxiety and/or depression.[1] However, less than 15 percent of respondents reported any expenses for mental health services, suggesting an unmet need in the AD community for increased mental health assessment and treatment in tandem with treatment for AD.[1] In the 2019 More Than Skin Deep report, several people with eczema articulated the interconnectedness of anxiety and depression with AD. Greg Clark, who lives with moderate-to-severe eczema reported that "eczema was controlling [him.]" He went on to say, "I got depressed. I was suicidal. I couldn't look at myself in the mirror because I didn't know who I was."[3] And Akilah Evans-Pigford, in reference to her teenage son's experience with eczema,

Figure 2. *Patient-reported financial impact on out-of-pocket costs related to atopic dermatitis.*

ECZEMA BY THE NUMBERS

Eczema is Expensive:

New Research by NEA Reveals the Out-of-Pocket Costs of Eczema

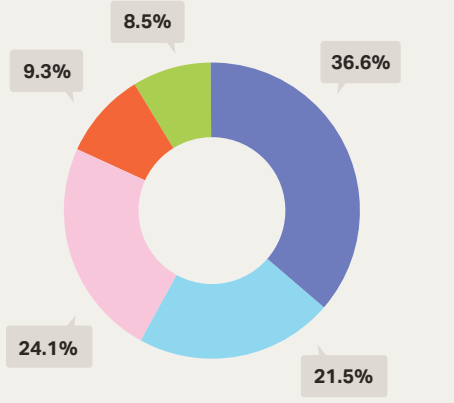
We know living with eczema comes with many costs. But, until recently, we did not know the extent of financial costs that Americans bear out of pocket (OOP) to manage their atopic dermatitis (AD).

The NEA research team set out to fill this gap with a survey of its eczema patient and caregiver community. The findings, analyzed in collaboration with researchers Dr. Raj Chovatiya, PhD (Northwestern University) and Dr. Jonathan Silverberg, PhD, MPH (The George Washington University School of Medicine and Health Sciences), have been published (in part) in Dermatitis.[1]

This study highlights the real-world costs of eczema and the importance of patients and their healthcare providers creating treatment plans that minimize financial burden while improving disease and quality of life outcomes.

For more information about this study and other research conducted by NEA, visit: NationalEczema.org/surveys

The financial burden of eczema is high for patients and caregivers.



Patients and caregivers spend in multiple categories and purchase multiple products — many not covered by insurance — to manage the diverse and unpredictable symptoms of eczema.

68.7% of respondents reported OOP copays and/or deductibles for visits to their healthcare provider(s) over the past 30 days

89.6% of responders had at least one prescription to treat their AD, while **57.5%** percent had three or more different prescriptions

Nearly half **(48.6%)** of AD patient and caregiver respondents had OOP costs for prescriptions not covered by insurance

94.3%, paid OOP for non-prescription, over-the-counter moisturizer

15.9% reported OOP expenses for adjunctive therapies (acupuncture, yoga, other relaxation approaches)

36.5%

of respondents reported diagnoses of anxiety and/or depression, yet only 14.4% reported expenses for mental health services

People with eczema often deal with anxiety and depression, yet few report expenses related to mental health

[1] Smith Begolka W, Chovatiya R, Thibau I, Silverberg J. Financial Burden of Atopic Dermatitis Out-of-Pocket Health Care Expenses in the United States. *Dermatitis*: 2020; 10.1097/DER.0000000000000715

explained that "After a while it got to the point where my son said things like, 'I hate myself,' and 'I don't want to be here anymore.'"[3]

THE IMPACT OF ECZEMA OOP

A majority of respondents (57.5%) in the survey indicated that they are using at least three different prescription treatments to manage their condition, highlighting the challenge of managing a chronic disease with periodic flares, but also the potential for increased OOP depending on insurance coverage.

For Ashtan Raniga, who lives with moderate-to-severe AD, the most surprising OOP expense was the cost of the medicine itself. "My medications for eczema tend to be around $30 every month," he said. "But without insurance that cost jumps to $300." Raniga explained that the burden of cost is compounded for people with multiple medications. "If you're someone like me," he said, "who has different types of flaring and a variety of medications, the cost can truly damage your financial well-being." Raniga added: "Some people have to decide between food on the table or taking care of their health. It's a lose/lose situation."

Patricia Cervini expressed a similar sentiment about the OOP costs of her treatment plan. "The first time I tried to get insurance approval for my medication," she said, "I vividly recall telling the pharma sales rep that I was willing to pay out of pocket if my insurance didn't approve the medication – I was that desperate. But when she quoted me the cost, I almost dropped the phone. Honestly, there was no way I could cover that cost every month."

Most survey respondents (40.1%) reported a moderate impact of these OOP expenses on their finances. However, nearly one-quarter (24.5%) indicated a significant or devastating effect. There was also a significant association with lower income and the use of Medicaid with increased negative impact of OOP costs for AD treatment *(Figure 2)*.[2]

ADDITIONAL UNDERREPORTED OUT-OF-POCKET COSTS

Analysis of survey responses revealed additional OOP costs independent of paying for prescriptions and co-pays, such as expenses for specialized clothing, bedding, and care-related transportation.

Amberley Sanden provides care for her 18-month-old brother, who also lives with moderate-to-severe eczema. "My baby brother has to wear 100% organic cotton to avoid flaring. He flares when he touches car seats, stroller seats, really anything," she said. "No matter the weather, he has to wear clothes that cover almost every inch of his body to avoid flaring, and since his clothing has to be right for him, that gets really expensive over time."

Patricia Cervini articulated the challenge of transportation-related costs. "While dupilumab was a miracle drug for my body, I still had stubborn flares within my eyebrows and around my eyes, so I tried phototherapy" she said. "My insurance covers the treatment, but the drive was two hours roundtrip, three times a week – and that's not sustainable." Patricia said she tried multiple times without success to get her insurance company to approve reimbursement for a phototherapy machine to use at home. "I was denied every time," she said. "In the end, I bought the smallest, most affordable phototherapy unit I could for my home, all out of my own pocket."

Ashtan Raniga mentioned the time and cost of driving as well. "In Northern California, the Kaiser Permanente locations are pretty spread out," he said. "With gas approaching $5 per gallon, the amount of money I spend traveling 35 miles each way to the doctor's office is really frustrating."

CONCLUSION

In summary, the data and details of NEA's research have outlined key opportunities for current health care conversations as well as future investigation. In a condition with complex, heterogeneous symptoms, the OOP financial burden is significant in how it universally affects people with all severities of AD, but especially those with uncontrolled disease, or severe AD. . While additional studies are needed to better understand the longitudinal associations of OOP costs and impacts, healthcare providers have an opportunity to use this information today to guide care decision making with their patients to minimize financial impacts of care while striving to achieve better disease control.

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Steve Nelson *is Senior Editor, National Eczema Association in Novato, California.*

Disclosures: *The author has disclosed no potential conflicts of interest, financial or otherwise, relating to the content of this article.*

Address for correspondence: *Steve Nelson; E-mail: steve@nationaleczema.org*

The Legal and Audit Perspective of the Patient Medical Record

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 next installment of Compliance Corner in which we will discuss the legal and audit perspective of the patient medical record. We also feature a reader question.

From "Quantifiable" to "Medically Appropriate"

What does this mean and why is it at issue?

One significant change seen in the 2021 E/M guidelines for office and outpatient services is that "quantifiable elements" for history and exam are no longer required. The new guidelines require a "medically appropriate" history and exam. To discuss best practices for compliant documentation to support these new guidelines, we must first ask what this change means and what is at issue. Why does this "new" statement cause confusion? Why is there concern about the history and exam documentation? How is the information contained in medical records intended to be used and, do these new guidelines change these intents?

Typically, medical records are used as evidence in Professional Misconduct Prosecutions, lawsuits, hearings, or inquests, as components of external reviews, audits, and peer assessments, and in billing investigations. Going back to before 2021 and looking at the prior documentation guidelines, we can read what the expectation was for medical record documentation. The 1995 and 1997 Documentation Guidelines both made the following statement concerning medical record documentation of the patient encounter:

Medical record documentation is required to record pertinent facts, findings, and observations about an individual's health history, including past and present illnesses, examinations, tests, treatments, and outcomes. The medical record chronologically documents the care of the patient and is an important element contributing to high quality care. The medical record facilitates:

- the ability of the physician and other healthcare professionals to evaluate and plan the patient's immediate treatment, and to monitor his/her healthcare over time
- communication and continuity of care among physicians and other healthcare professionals involved in the patient's care
- accurate and timely claims review and payment
- appropriate utilization review and quality of care evaluations; and collection of data that may be useful for research and education.

Do we believe any of this intent has changed with the 2021 documentation guidelines?

The 1995 and 1997 guidelines went on to further

state what was anticipated to be a part of the patient medical record.

The principles of documentation listed below are applicable to all types of medical and surgical services in all settings. For Evaluation and Management (E/M) services, the nature and amount of physician work and documentation varies by type of service, place of service and the patient's status. The general principles listed below may be modified to account for these variable circumstances in providing E/M services.

1. The medical record should be complete and legible.

2. The documentation of each patient encounter should include:

- reason for the encounter and relevant history, physical examination findings, and prior diagnostic test results; (Medically Appropriate)
- assessment, clinical impression, or diagnosis; (Problems Addressed)
- plan for care; (Risk)
- date and legible identity of the observer.

3. If not documented, the rationale for ordering diagnostic and other ancillary services should be easily inferred. (Data)

4. Past and present diagnoses should be accessible to the treating and/or consulting physician.

5. Appropriate health risk factors should be identified.

6. The patient's progress, response to and changes in treatment, and revision of diagnosis should be documented.

7. The CPT and ICD-9-CM codes reported on the health insurance claim form should be supported by the documentation in the medical record.

Why was this changed?

The 1995 and 1997 guidelines noted above really do seem to make good sense. They make sense clinically too. So, why has it changed?

The verbiage from the 1995 and 1997 guidelines became a formula that required quantification of how much history and how much exam, which led to a lot of confusion and even anger.

In the 2021 guidelines developed by the AMA, the medical record is still a legal record that should reflect the encounter with the patient. This legal health record should be able to achieve the following:

- Support the decisions made in a patient's care
- Support the revenue sought from third-party payers
- Document the services provided as legal testimony regarding the patient's illness or injury, response to treatment, and caregiver decisions
- Serve as the organization's business and legal record

Does any of this change with the 2021 documentation guidelines?

The guidelines now suggest a medically appropriate history and exam to be documented when and if performed. Contrary to the old guidelines, the amount of history obtained and documented, and the amount or extent of exam performed and documented does NOT affect the final level of service for office visits (99202 – 99215).

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Your Burning E/M Coding Questions... ANSWERED

Question: *I would like to make sure I am clear on one issue for 2021 E/M coding: If a patient comes in with a chief complaint of a new skin lesion that is documented in the HPI, then this lesion is biopsied, I know this visit becomes a procedural code only. However, let's say after the biopsy the patient inquired about another lesion that is then diagnosed as a normal lesion, let's say a seborrheic keratosis. They are counseled and reassured, and this plan is documented in the chart. However, because it was not a presenting problem, the provider did not go back and add this problem's history/description to the HPI. Can this still be considered a 99212 office visit or must there be an HPI element for the seborrheic keratosis to be considered an addressed problem for the E/M code?*

Answer: *If the documentation would reflect that the SK was examined or a comment is made that it was looked at and it is noted that the patient asked about it and the discussion with the patient and reassurance is documented then this would support a separate visit with the 25 modifier. I believe you are correct it would be a 99212.*

COULD THE SKIN LESION YOU'RE SEEING... ACTUALLY BE A DEADLY BLOOD CANCER?

LOOK FOR SKIN LESIONS

BPDCN lesions can vary in size, shape, and color.[1,2]*

YOU PLAY A CRITICAL ROLE IN EARLY AND ACCURATE DIAGNOSIS OF BPDCN

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an aggressive and deadly hematologic cancer with skin lesions that may be mistaken for other skin disorders.[1,2]

WHO ARE PATIENTS WITH BPDCN?

- **~85% to 90%** present with skin lesions[2-4]
- **~75%** are men[2,5]
- Typically between **60 to 70** years of age, but all ages can be affected[2,5]

Plasmacytoid dendritic cells invade the dermis where they proliferate, resulting in skin lesions that take the form of[1-3,6]:

- Nodular lesions
- Diffuse bruise-like macules

Research has uncovered key markers, including CD123, that allow for the proper diagnosis of BPDCN.[6†]

For more information, **visit BPDCNinfo.com.**

WHEN BIOPSYING APPROPRIATE SKIN LESIONS, ASK YOUR PATHOLOGIST TO CONSIDER CD123.‡

*Left image republished with permission from *Blood*; right image reprinted by permission from *Springer Nature: Modern Pathology, Neoplasms derived from plasmacytoid dendritic cells*. Facchetti F. © 2016.
†BPDCN diagnosis can include other markers, such as CD4, CD56, TCL1, and CD303 (BDCA2).[7]
‡Skin lesions associated with BPDCN may include violaceous nodules, bruise-like patches, or disseminated and mixed lesions (macules and nodules).[1,2]

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Does this guideline suggest that a history and exam is NOT necessary since it has no bearing on the level of service?

The question to ask in response must be…Is this a legal or a coding/auditing question? To help decide our answer, we should consider what Medicare has stated in the past few years about the expectation of documentation in the medical record for office and other outpatient visits (99202 – 99215). This information can be found in the CMS Final Rule that is published in the late fall of each year and provides guidance for the following year.

CMS made the following statement, which went into effect in 2019 and remains in effect:

> *For established patient office/outpatient visits, when relevant information is already contained in the medical record, practitioners may choose to focus their documentation on what has changed since the last visit, or on pertinent items that have not changed, and need not re-record the defined list of required elements if there is evidence that the practitioner reviewed the previous information and updated it as needed.*
>
> *Practitioners should still review prior data, update as necessary, and indicate in the medical record that they have done so.*
>
> *Additionally, we are clarifying that for E/M office/outpatient visits, for new and established patients for visits, practitioners need not re-enter in the medical record information on the patient's chief complaint and history that has already been entered by ancillary staff or the beneficiary. The practitioner may simply indicate in the medical record that he or she reviewed and verified this information.*

CMS made the following statement to go into effect in 2021;

> *The clinically outdated system for number of body systems/areas reviewed and examined under history and review will no longer apply, and the history and exam components will be performed when they are reasonable and necessary and clinically appropriate.*

These statements allow us to have some understanding of the expectation of what is in the medical record and who may record that information. Consider the following thoughts and really think about how your own documentation may look to an auditor:

1. Has the provider documented their review of information documented by others?

2. Do we know who documented what in the medical record?

a. History, exam, and medical decision making (MDM)

3. For established patients, is it clear in the documentation what has changed or what pertinent information has not changed?

4. Who determines what is "relevant?"

5. Who determines what is "medically appropriate?"

a. Who should?

Documentation Risks

There are risks when documentation in the patient's medical record does not clearly identify who documented the record and if the provider reviewed and updated information that had been entered by someone else. These new guidelines place less emphasis on the history and exam portion of the medical record. Does this imply that the legal aspect of the medical record has become less important? Consider these questions at your next practice meeting with compliance or legal or with your auditors. How should each of these statements be handled in an audit situation? The answers may vary based on if it is a clinician, auditor, compliance or legal, answering the question.

- What to do with contradictory information found in parts of history and exam
  - o Edema
  - o Past complaints, now resolved, per assessment and noted as positive in hx
- Cloned notes (hx and exam)
- Copy and Paste (hx and exam)
- No documentation to support the conditions noted in the assessment
- No current date of service (DOS information for the patient

Final Thoughts

When working with your compliance department, you may want to address the following items:

- ✔ Update any current policy concerning documentation to address language from the final rule 2019-2021
- ✔ Create a policy if needed
- ✔ Involve the medical director for consideration of "medically appropriate"
- ✔ Is there a policy addressing cloning?
- ✔ Involve the group

✔ When working or meeting with your auditing team or coding team you may want to discuss the following;

1. Make sure everyone understands any policies from compliance prior to starting the audit.

2. Clearly state how the information in the history and exam will be "handled" during the audit.

3. If there are concerns based on the documentation found in the history and exam, how will those be addressed?

The medical record remains a legal record that should accurately reflect the encounter between the patient and the provider. This is true regardless of payer documentation guidelines. However, these guidelines do make have an impact when someone reviews your documentation to support a level of service. Consider what your documentation is saying about the status of the patient and the care you are providing on that date of service.

Thank you and happy documenting!

Jaci J. Kipreos, CPC, CPMA, CDEO, CEMC, COC, CPCI, *has been working in the field of medical coding and auditing for over 30 years. She has been a Certified Professional Coder (CPC) since 1994, attained her Certified Outpatient Coder (COC) for facility-based coding in 2005, and is a Certified Professional Medical Auditor specializing in Evaluation and Management (E/M) Coding. She has expertise in coding for family practice, urgent care, obstetrics and gynecology, general surgery, and Medicare's Teaching Physician Guidelines, with a particular emphasis on E/M guideline compliance. She has served on the American Academy of Professional Coders (AAPC) National Advisory Board and is past president of AAPC's Richmond and Charlottesville, Virginia, local chapters. Kipreos is president of Practice Integrity, LLC, where she manages a national client list and provides compliance monitoring for provider documentation. She currently resides in San Diego, California.*

Disclosures: *The author has disclosed no potential conflicts of interest, financial or otherwise, relating to the content of this article.*

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

Cannulas for Dermal Filler Placement: *A Safety Review*

By Brittany Zimmerman, MPA-C

ABSTRACT

Over the last 10 years, the demand for nonsurgical aesthetic procedures has soared. Among these procedures, volume enhancement with soft tissue dermal fillers continues to be popular. New soft tissue dermal fillers are getting approved by the United States (US) Food and Drug Administration (FDA) and becoming available on the US market yearly. Traditionally, soft tissue fillers have been supplied and injected with hypodermal needles, however, the FDA has recently approved several soft tissue dermal fillers with the use of a cannula for injection. It is thought that cannulas may reduce injection complications, however, even with a blunt-tipped cannula patients can still suffer from tragic complications of vascular compromise leading to ischemia and blindness. It is essential that injectors understand the appropriate safety techniques to help avoid complications by learning how to determine whether a cannula is a better choice than a hypodermal needle when injecting and what to do if an intravascular event occurs.

KEYWORDS

Cannula, safety, dermal filler, hypodermic needle, filler complications, intravascular event, blindness

INTRODUCTION

Soft tissue filling is achieved using either a hypodermic needle or a cannula.[1] Hypodermic needles are non-flexible and have a sharp tip with the opening for the product at the distal cutting edge.[1] Cannulas have blunt and rounded tips, a distal opening for product delivery on one side, and may have flexible bodies.[1] Both needles and cannulas pose risks for complications. Minor complications include bruising, swelling, pain, and erythema.[2] More severe complications include infections, dermatitis, migration, granuloma formation, skin necrosis, pulmonary embolization, stoke, and blindness.[2]

Vascular compromise leading to ischemia and blindness is one of the most severe complications that can occur with dermal filler. These are caused by injection of the dermal filler material directly into a vessel or adjacent to a small vessel with a fixed structure behind.[3] The incidence of vascular occlusion following intravascular injection has been estimated at 3 per 1000 for calcium hydroxylapatite (CaHA) and 3-9 per 10,000 for hyaluronic acid (HA) products.[4] The true incidence of this complication is unknown because of underreporting by clinicians.[4] In a case review published in Aesthetic Plastic Surgery, of the 190 cases of blindness due to soft-tissue fillers 53 cases were caused by HA. The remaining cases were from autologous fat, collagen, CaHA, and other fillers.[4] The most common site of ocular complications involved with injections is at the nasal ala followed by the glabella region. In total, 90% of ocular complications occur after injections are made into the glabella, nose, forehead, and periocular region.[2]

LITERATURE REVIEW

The gauge of the needle/cannula is important when considering safety.[1] Pavicic et al[1] conducted a study to investigate whether different-sized cannulas are safer than correspondingly sized needles for the application of facial soft-tissue fillers. They discovered that there is no statistical difference between the mean force required to penetrate an artery on the left versus right side of the face, to penetrate the anterior branch of the superficial temporal artery versus the facial artery, or to penetrate an artery of a man versus a that of a woman. The study showed that increased age significantly correlated with a reduction in the force required to penetrate an artery.[1] There was also a correlation with the size of the needle. The smaller needles required less force to penetrate the arterial wall than large needles.[1] They found that when comparing same-sized cannulas and needles, 22- and 25-gauge cannulas required significantly more force to penetrate the arterial wall compared to 22- and 25-gauge needles, however, no statistical difference was found when comparing 27-gauge needles to cannulas.[1] This supports the theory that 27-gauge cannulas or smaller have the same risk as needles for vascular penetration, and 25-gauge and larger cannulas have lower risk over needles for vascular penetration.

In a recent article published in Plastic and Reconstructive Surgery journal, Zhou et al reported that over the course of three years, 25 of the 28 severe HA-related intravascular events referred to their department were performed with cannulas instead of needles.[5] The authors suggested that, given these findings, the safety of cannulas with HA injections may have been overestimated. They discussed many possible reasons for this overestimation. Previous studies propose that, because of different designs by varying manufacturers, some cannula tips are sharper than others with the same gauge. Poorly made cannulas have a rougher internal lining that can prevent successful aspiration therefore giving a false impression of safety. It is thought that aspiration can be more difficult with cannulas than with needles because there is a higher negative

pressure and longer aspiration time required for filler to retreat to the cannula base than in needles. Products with higher viscidity and larger particle size require a large bore and a longer aspiration time.[5]

Needles have been thought to be more precise for placing fillers than cannulas at the periosteum.[6] A study published in the Journal of Drugs in Dermatology showed that injections with cannulas were more accurate for product placement when compared to needles.[7] They showed a 33.3-percent increase in filler displacement towards more superficial layers when using a needle compared to a cannula. The researchers concluded that cannulas result in more precise placement of soft tissue fillers.[7] A study published in Aesthetic Surgery Journal concluded that all facial sites showed that a sharp needle used for product placement with the needle perpendicular to the skin resulted in product being placed in several layers of the tissue, whereas when a cannula was used for placement, the product remained confined to significantly fewer anatomic layers.[6]

DISCUSSION

Even in the most experienced hands, complications are not completely avoidable, but many prevention techniques have been discovered.[4] Injectors should have a solid knowledge of the underlying anatomy to understand what vessels are in the area of injection.[4] Injectors should use extended aspiration time (greater than 5 seconds) to allow filler to retreat to the base of the needle or cannula.[5,8] Cannulas tend to be longer in length than the supplied hypodermic needles; therefore, it will take longer for blood to enter the syringe if the needle or cannula had entered into a vessel.[8] Other techniques include using a slow-low pressure when injecting, continually moving the needle or cannula while injecting, and injecting small amounts of filler at a time.[4] Injectors should be observing for skin changes during injection and in the immediate post-injection period to allow for early intervention if required.[4]

In the case that an intravascular event occurs, the goal is to restore blood flow to the affected area immediately. The current treatment with HA fillers is to flood the affected area with copious amounts of hyaluronidase (at least 300-1500 IU depending on the amount of area involved and the severity of the incident) as soon as the diagnosis is made and repeated every one to two hours until significant improvement or reversal is seen.[4,9] The area can be massaged to facilitate spread of hyaluronidase, and a warm compress should be applied to increase vascular dilation and blood flow. Topical nitroglycerin (NTG) paste has been shown to instigate vasodilation and could reduce the risk for necrosis.[9] However, this treatment should be used with caution because orthostatis has been associated with its use. Oral aspirin, 650 mg daily for 1 week, may prevent further colt formation and is recommended to be administered for 1 week.[9]

CONCLUSION

Detrimental adverse events can occur any time soft tissue dermal filler is injected. Cannulas have been shown to cause fewer minor complications when compared to needles.[10] There may be a benefit to using greater than 25-gauge cannulas when in a high-risk area for vascular occlusion because cannulas require significantly more force to penetrate the arterial wall than needles of the same gauge.[1] Filler placement is more accurate when using a cannula and should be considered when injecting in areas where superficial displacement is a concern.[11]

The use of soft tissue dermal fillers will likely continue to increase due to the limited recovery time, accessibility of the procedure, and relatively affordable cost. Even in the most experienced hands, complications can occur. Injections using cannulas and needles have both been shown to cause catastrophic complications. It is important that injectors know the anatomy and what safety protocols to follow to prevent these events.[4] Moreover, it is essential that injectors know how to intervene if they see these events occurring.[7]

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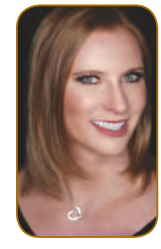

***Brittany Zimmerman, MPA-C**, is from A.T. Still University Arizona School of Health Science Doctor of Medical Science Program in Mesa, Arizona.*

***Disclosures:** The authors have disclosed no potential conflicts of interest, financial or otherwise, relating to the content of this article.*

***Address for correspondence:** Brittany Zimmerman, MPA-C, E-mail: number2ginger@gmail.com*

Listening To Patients
One Dollar and Forty-Two Cents

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."

No good deed goes unpunished.

We froze Myrna's keratosis off her forehead. Gratis, of course.

This was followed by repeated calls from Myrna: the spot was red, it was painful, it wasn't healing right.

So, we mailed her an envelope filled with cream to help heal the skin. Although we used our regular postage meter, somehow Myrna got the package with $1.42 postage due.

Not going to work.

Myrna called to complain. Then she drove over and walked into the office, but we weren't there. Then she called again and left a message. "I'm coming in this afternoon," she said. "I expect to pick up my $1.42."

Really.

Later that morning, Stephanie came by for a skin check. Because Stephanie is Catering Manager at a downtown ultra-upscale hotel, I knew she would both appreciate the tale of $1.42 and be able to top it. Everyone in her field can fill several books of client encounters no one could make up.

When I asked her to share some stories, Stephanie did not disappoint.

"Sure," she said. "People plan lavish weddings, no expense spared. But when they send gift baskets, we have to charge $3.50 each to pay the livery people who deliver them. That they object to."

"But what's even worse," she went on, "is when it comes to feeding the band. We discount the meals for musicians 60-70% below the per-plate rate for guests."

"That's not low enough for some people, though. We explain to them that the band members do have to eat. 'Yes,' say some of the brides, 'but do we have to give them a whole meal? Can't we just give them a sandwich or something?' This is from people who are spending six figures on food alone."

"Sounds like Marie Antoinette," I said. "What do you tell them?"

"We say, OK, we'll see if we can discount the band meals even more," Stephanie said.

Not an hour later, Ken came in. Ken manages an art-house movie theater in a close-in, affluent suburb. As I knew he would, Ken had stories too.

"People are always angling for some kind of special privilege," he said. 'I've been a patron for years," they say. 'Can't you do something for me?'

"What do they want?" I ask. "Free tickets?"

"Yes, or preferential seating," said Ken, "but we tell them that if we do that for them, we'd have to do it for everybody."

"Or else it's a cold, winter night and the theater is a little chilly. Some of the patrons want us to give them free popcorn." Ken sighed.

Anybody in the service business is going to meet up with behavior like this. We probably should be grateful that most patients have enough respect for our profession to dissuade them from:

- Demanding to be seen for free or have us waive the co-pay since "the treatment didn't work."
- Refusing to hand over the co-pay for a follow-up, because, "It was just a quick check, didn't take any time."

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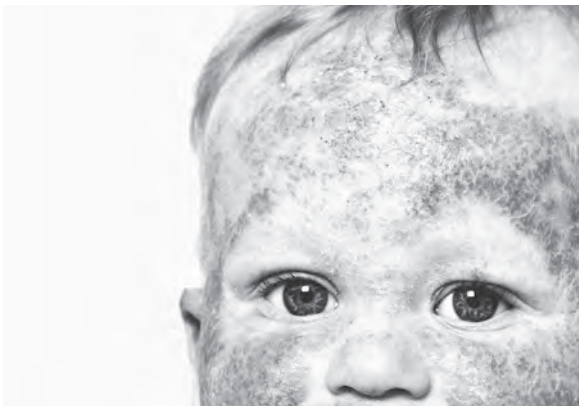

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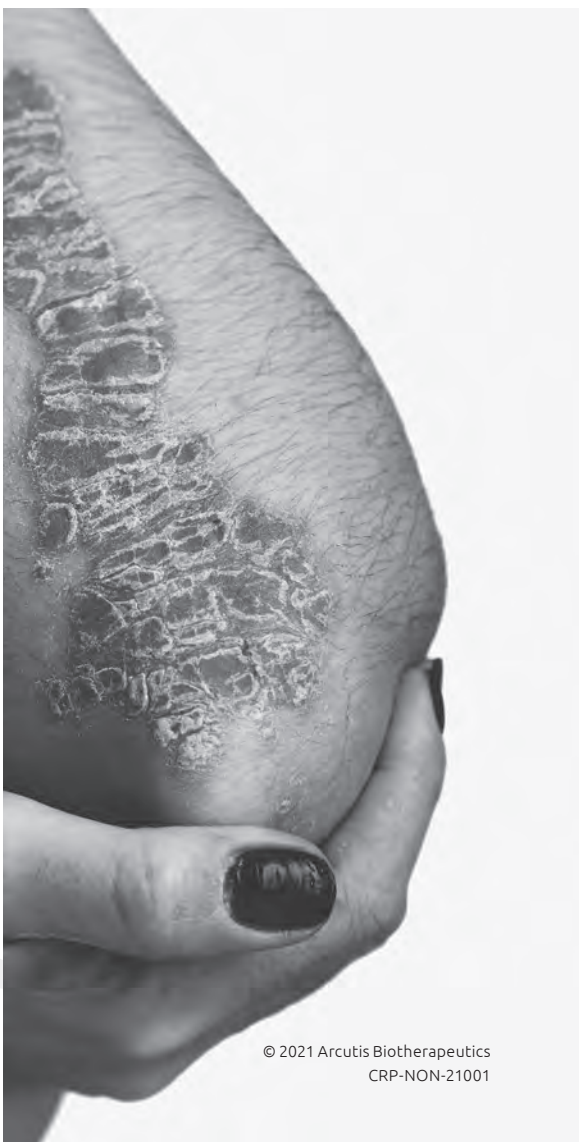

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• Insist on having us treat the wart or skin tag again at no charge, because "you missed a spot."

And so on. At least even our demanding patients don't ask for popcorn.

Myrna did show up that afternoon, by the way. I don't know how much she spent on gas to come in.

My Office Manager Amina took care of things. She gave Myrna her buck-42:

Three quarters.

Two dimes.

Five nickels.

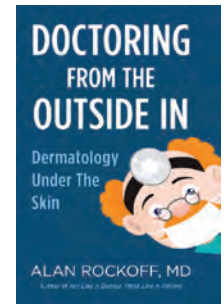
And 22 pennies.

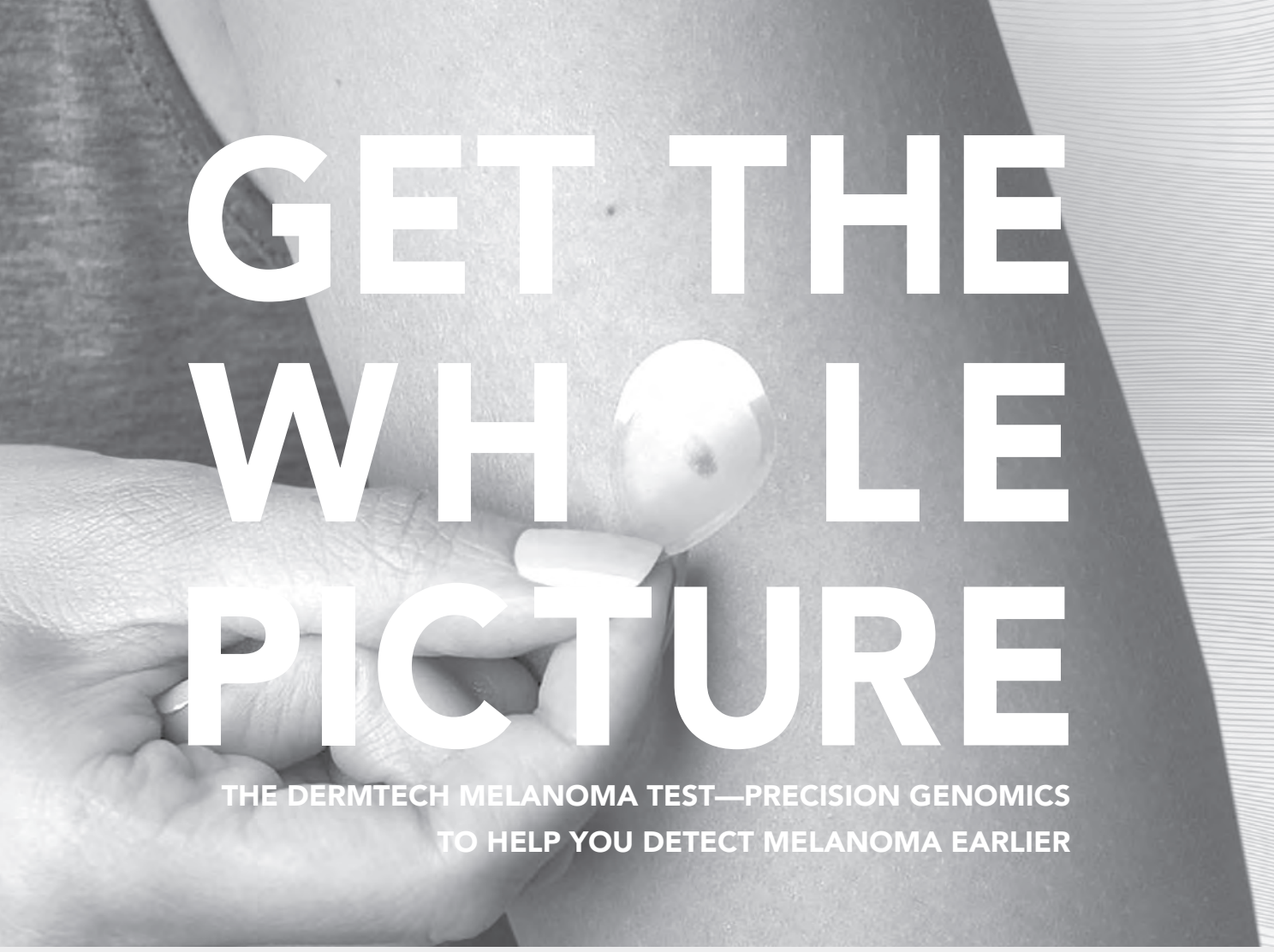
Amina is really good at keeping a straight face.

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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SDPA Annual Summer Conference 2021 – A Hybrid Experience

The Society of Dermatology Physician Assistants (SDPA) returned to the in-person continuing medical education conference scene this past summer, hosting the SDPA Annual Summer Dermatology Conference 2021 on July 22-25, 2021, at Chicago Marriott Downtown Magnificent Mile in Chicago, Illinois. The conference marked the society's first ever hybrid conference, which offered attendees the choice to participate in-person (live), virtually (live streamed), or on-demand following the event. Despite the ongoing pandemic and news of the delta variant just emerging, live conference participants—attendees, faculty, leadership, staff, and industry partners—exuded a collective excitement to be "back;" and the city of Chicago, seasonably warm and bustling with tourists, seemed to welcome everyone with equal enthusiasm.

SESSION HIGHLIGHTS

Integrative Dermatology.

Peter Lio, MD, Clinical Assistant Professor of Dermatology & Pediatrics at Northwestern University Feinberg School of Medicine and physician at Medical Dermatology Associates of Chicago in Chicago, Illinois, served as Summer Conference Medical Director. Dr. Lio, a Chicago native, could be seen on stage delivering multiple presentations and around the conference venue making new connections. He gave back-to-back sessions on two unique, connected topics—Integrative Dermatology and Cannabinoids in Dermatology. He shared evidence behind integrative approaches in dermatology for a variety of common conditions, including psoriasis, warts, and acne, as well as insight into why many patients seek integrative or alternative therapies. Several case descriptions revealed that patients are often "phobic" of Western treatments

like steroids, topical calcineurin Inhibitors, antibiotics, and anything containing Preservatives (e.g., parabens), or chemicals. Some alternative therapies discussed included the following:

- **Psoriasis:** fish oil and indigo
- **Acne:** tea tree oil, spearmint tea, vitamins (niacinamide, Pantothenic acid [vitamin B5]), and physical modalities (e.g., PDT, blue light/red light alone, chemical peels, extractions, other lasers and light sources)
- **Warts:** propolis, zinc, and garlic

- **Atopic Dermatitis:** acupuncture, acupressure, coconut oil, topical B12, black tea compresses, hempseed oil

Transgender Medicine.

Tiffany Pierce, PA-C, began her presentation with a simple slide stating, "Transgender Medicine, The Dermatology Version" and a bulleted list of credentials: transgender PA, special forces medic, laser guru (self-designated), state and national medical conference dermatology presenter/speaker, and lecturer/speaker on dermatology at PA programs. Ms. Pierce, provided a basic overview of gender dysphoria, intersex conditions, sex-ual minorities, sexual orientation, gender identity, and gender expression. Her talk illustrated the significant positive impact dermatology can have for transgender patients.

Winner! Congratulations to Lauren Wilson, MMS, PA-C, of North Carolina, who won a DermLite Dermatosope upon locating Sherman the Snake.

Everyone embraced the Roaring 1920s-theme with style and had a blast learning the Charleston at The Last Speakeasy event.

Perils of Penile Pathology.

SDPA Founder and past president Joe Monroe, MPAS, PA-C, covered common and not-so-common penile conditions and lesions, in a two-part series designed especially for providers who seldom see this part of the male anatomy. Featuring photos from his own 35-year collection, Mr. Monroe approached the topic with expertise and a little humor. He engaged the audience with question-and-answer slides on various penile conditions. One important take-home message from these lectures was that yeast infections of the penis or surrounding areas are "quite uncommon and vastly over diagnosed," therefore, dermatology clinicians should consider the differential diagnoses first.

Bright Lights! Big City!

SDPA was delighted to have been joined by 700+ dermatology PAs and professionals in person and virtually from around the country. For those onsite, SDPA Annual Summer Conference was as entertaining as it was educational. Onsite attendees quickly caught on to the popular Where's Sherman? contest, arriving early to search the lobby and ballroom for Sherman the snake, the flashy reptile who escaped his spot on the SDPA logo. Attendees who found Sherman, a plush stuffed animal hidden each day of the conference, traded him in for a DermLite Dermatoscope. There were also plenty of opportunities to socialize and network. One memorable event was The Last Speakeasy hosted at the Chicago InterContinental. Everyone embraced the Roaring 1920s-theme with style and had a blast learning the Charleston.

SDPA Annual Summer Conference 2021

Conference abstracts are available in both print and online versions of Journal of Dermatology for Physician Assistants (JDPA), Summer 2021 issue.

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SDPA Presents Fall 2021 Digital Abstracts
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1. Efficacy and Safety of Risankizumab (RZB) for Active Psoriatic Arthritis (PsA): 52-week Results From KEEPsAKE 1

Lars Erik Kristensen[1]; Mauro Keiserman[2]; Kim Papp[3]; Leslie McCasland[4]; Douglas White[5]; Wenjing Lu[6]; Ahmed M Soliman[6]; Ann Eldred[6]; Lisa Barcomb[6]; Frank Behrens[7]

[1]The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen, Denmark; [2]Rheumatology Section, Pontifical Catholic University, School of Medicine, Porto Alegre, Brazil; [3]Probity Medical Research–K Papp Clinical Research, Waterloo, Ontario, Canada; [4]Department of Rheumatology, Loyola University Medical Center, Maywood, Illinois, USA; [5]Rheumatology Department, Waikato Hospital, Hamilton, New Zealand; 6AbbVie Inc., North Chicago, Illinois, USA; 7CIRI/ Rheumatology, Goethe University, Frankfurt, Germany

Introduction: RZB, a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits the p19 subunit of the human cytokine IL-23, is being investigated as a treatment for PsA.

Methods: KEEPsAKE 1 (NCT03675308) is an ongoing, phase 3 study that includes a screening period; a 24-week double-blinded, placebo-controlled, parallel-group period (period 1); and an open-label extension period (period 2). Eligible patients aged ≥18 years with active PsA (symptom onset ≥6 months prior to screening, meeting the Classification Criteria for PsA [CASPAR], and ≥5 swollen and ≥5 tender joints) and who had an inadequate response or intolerance to ≥1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR), were randomized 1:1 to receive RZB 150 mg or placebo (PBO) at weeks 0, 4, and 16. The primary endpoint was the proportion of patients achieving ≥20% improvement in American College of Rheumatology (ACR20) response at week 24. Period 2 started at week 24, and patients were switched to receive open-label RZB 150 mg every 12 weeks through week 208. Mixed-effect model repeated measures and nonresponder imputation methods were used to assess continuous and binary variables, respectively. Efficacy and safety were analyzed in all patients who received ≥1 dose of study drug through week 52. Treatment-emergent adverse events (TEAE) were summarized using exposure-adjusted event rates (EAERs, events/100 patient-years [PY]).

Results: At week 24, a greater proportion of RZB-treated (N=483) vs PBO-treated (N=481) patients achieved ACR20 (55.3% and 32.8%, respectively). At week 52, 70% of patients who were randomized to receive RZB and 63% of patients who were randomized to receive PBO and switch to RZB at week 24 achieved ACR20. In patients with ≥3% of body surface area affected at baseline, 52.7% of RZB-treated patients (N=273) and 9.9% of PBO-treated patients (N=272) achieved ≥90% improvement in Psoriasis Area and Severity Index (PASI 90) at week 24; 67.8% who were randomized to receive RZB and 59.9% who were randomized to receive PBO and switch to RZB at week 24 achieved PASI 90 at week 52. Similar results were observed for other efficacy measures. RZB was well tolerated through 52 weeks of treatment. EAERs of adverse events were stable between weeks 24 and 52. At the week 52 data cut-off (19 April 2021), the total EAER of any TEAE in patients receiving RZB was 143.1/100 PY.

C**onclusion:** Continuous RZB treatment provided durable efficacy and a consistent safety profile through 52 weeks of treatment in patients with active PsA who were csDMARD-IR.

Presenting author: Lars Erik Kristensen, MD, PhD

Disclosures:

LE Kristensen has received honoraria or fees for serving as a speaker or consultant from AbbVie, Amgen, Biogen, Bristol Myers Squibb, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, and has received research grants from AbbVie, Biogen, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB.

M Keiserman has received honoraria or fees for serving on advisory boards, as a speaker, or as a consultant, and grants as a principal investigator from AbbVie, Amgen, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche, and UCB.

K Papp has received research funds from AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, Dermavant, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, Gilead, Incyte, Janssen, LEO Pharma, Lilly, Merck, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB. He is a consultant for AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, Dermavant, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, Gilead, Incyte, Janssen, LEO Pharma, Lilly, Meiji Seika Pharma, Merck, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB. He is a speaker for AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Incyte, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Sandoz, Sanofi Genzyme, and UCB, and is a committee member for PSOLAR (Psoriasis Longitudinal Assessment and Registry) and PURE (registry of patients with moderate-to-severe chronic plaque psoriasis in Latin America and Canada).

L McCasland has received fees for serving on an advisory board from Lilly.

D White has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant from AbbVie and Novartis.

W Lu, A Soliman, A Eldred, and **L Barcomb** are employees of AbbVie, Inc. and may hold AbbVie stock and/or stock options. A Soliman is a coinventor on AbbVie patents.

F Behrens has received research grants, honoraria, or fees for serving as a consultant or speaker from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Chugai, Galapagos, Genzyme, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, and Sanofi.

Funding: AbbVie, Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission. All authors had access to the data; participated in the development, review, and approval of the abstract. AbbVie and the authors thank the patients

who participated in the study and all study investigators for their contributions. AbbVie funded the research for this study and provided writing support for this abstract. Medical writing assistance, funded by AbbVie, was provided by Jay Parekh, PharmD, of JB Ashtin.

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2. Efficacy and Safety of Risankizumab (RZB) for Active Psoriatic Arthritis (PsA): 52-Week Results From KEEPsAKE 2

Andrew Östör,[1] Filip Van den Bosch,[2] Kim Papp,[3] Cecilia Asnal,[4] Ricardo Blanco,[5] Jacob Aelion,[6] Wenjing Lu,[7] Zailong Wang,[7] Ahmed M Soliman,[7] Ann Eldred,[7] Byron Padilla,[7] Alan Kivitz[8]

[1]Monash University, Cabrini Hospital, Melbourne, Victoria, Australia; [2]Department of Rheumatology, Ghent University, Ghent, Belgium; [3]Probity Medical Research–K. Papp Clinical Research, Waterloo, Ontario, Canada; [4]DOM Centro de Reumatología, Buenos Aires, Argentina; [5]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain; [6]Arthritis Clinic and West Tennessee Research Institute, Jackson, Tennessee, USA; [7]AbbVie Inc., North Chicago, Illinois, USA; [8]Altoona Center for Clinical Research, Duncansville, Pennsylvania, USA

Introduction: RZB, a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits the p19 subunit of the human cytokine interleukin-23, is being investigated as a treatment for PsA.

Methods: KEEPsAKE 2 (NCT03671148) is an ongoing, phase 3, multicenter study that includes a screening period; a 24-week double-blinded, randomized, placebo-controlled, parallel-group period (period 1); and an open-label extension period (period 2). Eligible patients were ≥18 years of age with active PsA (symptom onset ≥6 months before screening, meeting Classification Criteria for PsA [CASPAR], and ≥5 tender and ≥5 swollen joints) and had inadequate response or intolerance to 1 or 2 biologic therapies (Bio-IR) and/or ≥1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR). Patients received RZB 150 mg or placebo (PBO) at weeks 0, 4, and 16 (1:1). The primary endpoint was the proportion of patients achieving ACR20 response at week 24. Period 2 started at week 24, and patients were switched to receive open-label RZB 150 mg every 12 weeks through week 208. Efficacy and safety were analyzed in patients who received ≥1 dose of study drug through week 52. Mixed-effect model with repeated measures and nonresponder imputation methods were used to assess continuous and binary variables, respectively. Treatment-emergent adverse events (TEAEs) were summarized using exposure-adjusted event rates (EAERs, events/100 patient-years [PY]).

Results: At week 24, 49.6% of RZB-treated (N=224) and 27.9% of PBO-treated (N=219) patients achieved ACR20. At week 52, 58.5% of patients who were randomized to RZB and 55.7% of patients who were randomized to PBO and then switched to RZB at week 24 achieved ACR20. In patients with ≥3% of body surface area affected at baseline, 56.1% of RZB-treated patients (N=123) and 10.9% of PBO-treated patients (N=119) achieved PASI 90 at week 24. At week 52, 64.2% of patients randomized to RZB and 59.7% of patients who were randomized to PBO and then switched to RZB at week 24 achieved PASI 90. For other efficacy measures, similar trends were observed. RZB was well tolerated through 52 weeks of treatment, and EAERs of adverse events were stable between weeks 24 and 52. At the week 52 data cutoff (19 April 2021), the total EAER of any TEAE in patients receiving RZB was 184.2/100 PY.

Conclusion: Continuous RZB treatment resulted in maintained efficacy responses with a consistent safety profile through 52 weeks of treatment in patients with active PsA who were Bio-IR and/or csDMARD-IR.

Presenting author: Andrew Östör, MD

Disclosures:

A Östör has received speaker or consulting fees and/or research grants from AbbVie, Bristol Myers Squibb, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB.

F Van den Bosch has received speaker and/or consulting fees from AbbVie, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB.

K Papp has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, Lilly, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB.

C Asnal has received honoraria or fees for serving on advisory boards or as a speaker, as well as research support from AbbVie, Amgen, Genentech, Janssen, Lilly, Pfizer, Roche, and R-Pharm.

R Blanco has received grants or research support from AbbVie, Merck, and Roche. He has received consultation fees or honoraria for serving as a speaker for AbbVie, Bristol Myers Squibb, Janssen, Lilly, Merck, Pfizer, and Roche.

J Aelion has received grants or research support from AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Galapagos/Gilead, Genentech, GlaxoSmithKline, Lilly, Mallinckrodt, Nektar Therapeutics, Nichi-Iko, Novartis, Pfizer, Regeneron, Roche, Sanofi, Selecta Biosciences, and UCB.

W Lu, Z Wang, A Eldred, and **B Padilla** are full-time employees of AbbVie, and may hold AbbVie stock or stock options.

AM Soliman is a full-time employee of AbbVie, may hold AbbVie stock or stock options, and is a co-inventor on AbbVie patents.

A Kivitz is a shareholder of or has received honoraria or fees as a consultant, speaker, or expert witness for AbbVie, Boehringer Ingelheim, Celgene, Flexion, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB.

Funding: AbbVie, Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission. All authors had access to the data;

participated in the development, review, and approval of the abstract. AbbVie and the authors thank the patients who participated in the study and all study investigators for their contributions. AbbVie funded the research for this study and provided writing support for this abstract. Medical writing assistance, funded by AbbVie, was provided by Jay Parekh, PharmD, of JB Ashtin.

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3. Integrated Analysis of Long-Term Safety of Risankizumab in Patients With Moderate-to-Severe Plaque Psoriasis

Kenneth B. Gordon[1], Kim A. Papp[2], Hervé Bachelez[3], Andrew Blauvelt[4], Megha Shah[5], Brian Waterhouse[5], Ranjeeta Sinvhal[5], Kristian Reich[6]

[1]Medical College of Wisconsin, Milwaukee, USA; [2]K Papp Clinical Research and Probity Medical Research, Waterloo, Canada; [3]APHP Hôpital, Université de Paris, Paris, France; [4]Oregon Medical Research Center, Portland, USA; [5]AbbVie Inc., North Chicago, USA; [6]University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Introduction: We examined long-term safety of interleukin-23 inhibitor, risankizumab, in patients with moderate-to-severe plaque psoriasis in an integrated analysis of psoriasis clinical studies.

Methods: An integrated all-risankizumab safety data set was compiled from 17 completed or ongoing phase 1–3 clinical trials in plaque psoriasis (data cutoff October 12, 2020). Adverse events(AEs) and AEs of safety interest were assessed for patients receiving ≥1 dose of risankizumab. Treatment-emergent AEs were defined as any event with onset after first dose and within 140 days after last dose of risankizumab during analysis. Data are reported as number of patients with AEs and events per 100 patient-years (PYs); 95% CIs provided for grouped events.

Results: 3131 patients with 9081.2 PYs of risankizumab exposure were included. Median treatment duration was 3.3 years(yrs; range, 1 day to 6.4 years), with treatment duration ≥2yrs in 65.8% and ≥4yrs in 35.3% of patients. AEs were related to upper respiratory tract infection related. Rate of serious AEs remained stable at 7.7 events/100 PY; AEs of safety interest included serious infections, major adverse cardiovascular events (MACE), non-melanoma skin cancer (NMSC), malignancies excluding NMSC and serious HSRs. Rate of serious infections remained stable (1.3/100 PY). Most common serious infections included pneumonia and sepsis, which are common in PsO and general population. There were no cases of active tuberculosis. Rates of NMSC (0.7/100PY) and malignant tumors excluding NMSC (0.6/100 PY) were stable. Most common malignant tumors excluding NMSC were breast cancer, prostate cancer, and malignant melanoma in situ, common malignancies in the general population or identified in dermatology clinical practices. Among NMSC, most common were basal cell carcinoma (BCC, 39 events in 27 patients) and cutaneous squamous cell carcinoma (SCC, 18 events in 15 patients; BCC:SCC ratio of 1.8:1). All other malignant tumors were reported with <3 events each (<0.1/100 PY). Total of 51 adjudicated MACE (0.6/100 PY) were reported. Total of 5(<0.1/100 PY) serious hypersensitivity events were reported, none of which were considered related to risankizumab.

Conclusion: This integrated analysis of risankizumab safety data encompassed more than 3100 patients with over 9000 PY of exposure from the psoriasis clinical trial program. Findings show risankizumab is well tolerated with long-term treatment (up to 6.4yrs) in patients with moderate-to-severe psoriasis, with a low occurrence of AEs of safety interest.

Disclosures:

Kenneth B. Gordon has received honoraria for serving as a consultant and/or grants as an investigator from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly, GlaxoSmithKline, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron, Sanofi-Aventis, Sun, and UCB.

Kim A. Papp has received honoraria or fees for serving on advisory boards, as a speaker, or as a consultant, and grants as principal investigator from AbbVie, Amgen, Arcutis, Astellas, Avillion, Bausch Health, Baxalta, Baxter, Boehringer Ingelheim, Botanix, Bristol-Myers Squibb, Celgene, Coherus, Dermavant, Dermira, Eli Lilly, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa-Hakko Kirin, Leo Pharma, Meiji Sika Pharma, MedImmune, Merck-Serono, Merck Sharp & Dohme, Mitsubishi, Novartis, Pfizer, Regeneron, Roche, Samsung Biopepis, Sanofi-Genzyme, Stiefel, Sun Pharma, Takeda, UCB, and Valeant.

Here Bachelez has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant and grants as an investigator from AbbVie, Almirall, Amgen, Bayer, Baxalta, Biocad, Boehringer Ingelheim, Celgene, Dermavant, Eli Lilly, Janssen, Leo Pharma, Menarini, MSD, Novartis, Pfizer, Pierre Fabre, Sandoz, Sun Pharmaceuticals, and UCB.

Andrew Blauvelt has served as a scientific adviser 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, Janssen, Landos, Leo, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma.

Megha Shah and **Ranjeeta Sinvhal** are full-time employees of AbbVie and may own stock/stock options.

Brian Waterhouse is a former employee of AbbVie and may own stock/stock options.

Kristian Reich has served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Affibody, Almirall, Amgen, Avillion, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Covagen, Dermira, Forward Pharma, Fresenius Medical Care, Galapagos, Galderma, GlaxoSmithKline, Janssen-Cilag, Kyowa Kirin, Leo, Lilly, Medac, Merck Sharp & Dohme, Miltenyi Biotec, Novartis, Ocean Pharma, Pfizer, Regeneron, Samsung Biopepis, Sanofi, Sun Pharma, Takeda, UCB, Valeant, and Xenoport.

Acknowledgments: AbbVie funded this study, and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of

this publication. No honoraria or payments were made for authorship. Medical writing support was provided by Moira Hudson, PhD, and Janet Matsuura, PhD, of ICON (North Wales, PA, USA) and was funded by AbbVie.

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4. Long-Term Efficacy and Safety of Risankizumab for Treatment of Moderate-To-Severe Plaque Psoriasis: Interim Analysis of LIMMitless Open-Label Extension Trial Beyond 3.5 Years Follow-Up

Kim A Papp,[1] Mark G Lebwohl,[2] Lluís Puig,[3] Mamitaro Ohtsuki,[4] Stefan Beissert,[5] Jiewei Zeng,[6] Simone Rubant,[6] Ranjeeta Sinvhal,[6] Ahmed M. Soliman,[6] Stefan Beeck,[6] Craig Leonardi [7]

[1]K Papp Clinical Research &Probity Medical Research, Waterloo, Canada; [2]Icahn School of Medicine at Mount Sinai, New York, USA; [3]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [4]Jichi Medical University, Tochigi, Japan; [5]University Hospital Carl Gustav Carus, Dresden, Germany; [6]AbbVie Inc., North Chicago, USA; [7]Central Dermatology, Richmond Heights, USA

Introduction/Objectives: We evaluated long-term efficacy and safety of risankizumab, an IL-23 p19, humanized IgG1 monoclonal antibody, for treatment in adults with moderate-to-severe plaque psoriasis (PsO).

Methods: LIMMitless is an ongoing, phase 3 open-label extension(OLE) study(NCT03047395) evaluating long-term efficacy and safety of continuous risankizumab 150 mg (RZB150) treatment in patients with PsO. Patients who were randomized to receive RZB150 at week(wk) 0, 4, and every 12wks thereafter (total 24–52wks) in 5 double-blind, phase 3 base trials (UltIMMa 1/NCT02684370; UltIMMa 2/NCT02684357; SustaIMM/NCT03000075; NCT03255382; or IMMvent/NCT02694523), were candidates for long term RZB150 in the OLE study, continuing open-label RZB150 every 12wks. This interim analysis evaluated continuous RZB efficacy through 196wks and safety through data cutoff date (November 16, 2020; up to 224 weeks of treatment). Efficacy was assessed by proportion of patients achieving ≥90% or 100% improvement in Psoriasis Area and Severity Index(PASI 90 and PASI 100, respectively) and mean improvement in PASI from baseline. Other efficacy assessments included proportion of patients achieving static Physician's Global Assessment of clear or almost clear (sPGA 0/1) and Dermatology Life Quality Index of no effect on patient's life (DLQI 0/1). Efficacy was calculated using 3 methods to impute missing data (modified nonresponder imputation[mNRI], last observation carried forward[LOCF], and observed cases[OC]). Safety of continuous RZB treatment was assessed by monitoring reported adverse events (AEs) and was calculated as the number of events per 100 patient-years (PY) to account for differences in the base study lengths.

Results: Of 955 patients randomized to RZB150 in base trials, 897 continued into LIMMitless OLE study, and 766 were still ongoing at data cutoff date. After 196wks of continuous RZB150,patients achieved: PASI 90(83.5%), PASI 100(51.3%), sPGA 0/1(84.6%), and DLQI 0/1(76.1%), using the mNRI method for missing data imputation. These improvements, and the mean percent improvement in PASI from baseline, were generally reached by 52wks of continuous RZB150 and remained high and durable through 196wks of treatment. Results using the OC and LOCF methods were consistent with these findings. Rates of AEs and AEs of safety interest were low and consistent with those observed in base studies.

Conclusions: Patients receiving long-term continuous RZB150 treatment (every 12 weeks for 196 weeks) achieved high durable efficacy and quality of life improvements throughout the LIMMitless study. RZB was well tolerated through the time of data cutoff (up to 224 weeks of continuous treatment) with a safety profile similar to base studies profile with no new safety signals observed.

Presenting Author: Kim A Papp, MD, PhD

Disclosures:

KAP has received research funds from AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermavant, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, Gilead, Incyte, Janssen, LEO Pharma, Lilly, Merck, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB. He is a consultant for AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermavant, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, Gilead, Incyte, Janssen, LEO Pharma, Lilly, Meiji Seika Pharma, Merck, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB. He is a speaker for AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, Incyte, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Sandoz, Sanofi Genzyme, and UCB, and is a committee member for PSOLAR and PURE registries.

MGL is an employee of Mount Sinai and receives research funds from AbbVie, Amgen, Arcutis, Boehringer Ingelheim, Dermavant, Evommune, Incyte, Janssen, LEO Pharma, Lilly, Ortho Dermatologics, Pfizer, and UCB. He is a consultant for Aditum Bio, Allergan, Almirall, Arcutis, Avotres, BirchBioMed, BMD Skincare, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant, Dr. Reddy's Laboratory (Promius), EMD Serono, Evelo Biosciences, Evommune, Facilitate International Dermatologic Education, Foundation for Research and Education in Dermatology, Inozyme Pharma, Kyowa Kirin, LEO Pharma, Meiji Seika Pharma, Menlo Therapeutics, Mitsubishi Tanabe Pharma, NeuroDerm, Pfizer, Theravance, and Verrica.

LP has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Celgene, EMD Serono, Gebro, Janssen, LEO Pharma, Lilly, Merck, Mylan, Novartis, Pfizer, Regeneron, Roche, Samsung Bioepis, Sandoz, Sanofi, and UCB.

MO has received honoraria or fees for serving on

advisory boards, as a speaker, and as a consultant. He has received grants as an investigator from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eisai, Janssen, Kyowa Kirin, LEO Pharma, Lilly, Maruho, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Sanofi, Sun Pharma, Torii Pharmaceutical, and UCB.

SBeissert has received honoraria as an advisory board member for AbbVie, Actelion, Almirall, Amgen, Celgene, Galderma, Janssen, LEO Pharma, Lilly, Menlo Therapeutics, Merck, Novartis, Pfizer, Sanofi, and UCB and as a speaker for AbbVie, Actelion, Almirall, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Roche, and Sandoz.

JZ, SR, RS, AMS, and **SBeeck** are full-time employees of AbbVie Inc., and may hold AbbVie stock and/or stock options.

CL has received honoraria as a consultant/advisory board member for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Janssen, LEO Pharma, Lilly, Ortho Dermatologics, Pfizer, Sandoz, UCB, and Vitae Pharmaceuticals, and as a speaker for AbbVie, Amgen, Celgene, Lilly, Novartis, Sun Pharma, and UCB. He has received fees for service as a principal investigator for Actavis, Amgen, Boehringer Ingelheim, Celgene, Cellceutix, Coherus, Corrona, Dermira, Galderma, Glenmark, Janssen, LEO Pharma, Lilly, Merck, Novartis, Novella Clinical, Pfizer, Sandoz, Sienna Biopharmaceuticals, Stiefel, UCB, and Warner Chillcott.

Funding: AbbVie Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission. All authors had access to the data; participated in the development, review, and approval of the abstract. AbbVie funded the research for this study and provided writing support for this abstract.

AbbVie and the authors thank the patients who participated in the study and all study investigators for their contributions. AbbVie would also like to thank Saskia De Vente and Lawrence McNamee, both of whom are AbbVie employees, for their contributions to this study. Medical writing assistance, funded by AbbVie, was provided by Callie A S Corsa, PhD, and Jennifer C Jaworski, MS, of JB Ashtin.

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5. Abrocitinib Treatment in Patients With Moderate-to-Severe Atopic Dermatitis: Safety of Abrocitinib Stratified by Age

Michael J. Cork,[1] Mette Deleuran,[2] Bob Geng,[3] Jonathan I. Silverberg,[4] Eric L. Simpson,[5] Linda F. Stein Gold,[6] Susan Johnson,[7] William Romero,[8] Hernan Valdez,[9] Min H. Zhang,[10] Natalie Yin[9]

[1]Sheffield Dermatology Research, IICD, University of Sheffield, Sheffield Children's Hospital, Sheffield, UK; [2]Aarhus University Hospital and Aarhus University, Aarhus, Denmark; [3]UC San Diego School of Medicine, San Diego, CA, USA; [4]The George Washington University School of Medicine and Health Sciences, Washington DC, USA; [5]Oregon Health and Science University, Portland, OR, USA; [6]Henry Ford Health System, Detroit, MI, USA; [7]Pfizer Inc, Raleigh-Durham, NC, USA; [8]Pfizer Ltd., Tadworth, UK; [9]Pfizer Inc., New York, NY, USA; [10]Pfizer Inc., La Jolla, CA, USA

Introduction: Abrocitinib is an oral, once-daily, Janus kinase 1–selective inhibitor with demonstrated efficacy and safety in adults and adolescents with moderate-to-severe atopic dermatitis (AD), but safety by age has not been addressed directly. We analyzed safety data from clinical studies in patients with moderate-to-severe AD in various age groups.

Methods: Data were pooled from a phase 2b study (NCT02780167) and 6 phase 3 studies (NCT03349060, NCT03575871, NCT03720470, open-label period of NCT03627767, NCT03422822, and NCT03796676). This analysis included all patients who received ≥1 dose of abrocitinib 200 mg or 100 mg; adverse events (AEs) of interest and laboratory abnormalities were evaluated.

Results: Among 3128 patients, the total exposure was 2089 patient-years; 994 patients had ≥48 weeks and 346 had ≥72 weeks of exposure. The population comprised 635 (20%) patients aged 12 to 17 years, 1472 (50%) aged 18 to 39 years, 776 (25%) aged 40 to 64 years, and 145 (5%) aged ≥65 years. Although the proportions of patients with AEs were similar across age groups (range, 67% to 75%), serious AEs were more common in patients ≥65 years of age than in other age groups (13% vs 4%). The same was true for severe AEs (11% vs 6%) and AEs leading to discontinuation (19% vs 6%-10%). The numbers of patients per 100 patient-years with platelet count <75 × 103/mm3, lymphocyte count <0.5 × 103/mm3, and adjudicated opportunistic herpes zoster generally increased with increasing age and higher dose. Overall, most adjudicated opportunistic herpes zoster infections (80%) were mild or moderate; most (75%) resolved by the time of last observation. No clinical sequelae were observed in the context of these laboratory abnormalities; there was no association between lymphocyte and neutrophil count and risk of serious infection. Overall, age ≥65 years was generally associated with a higher risk of serious infections, malignancies (nonmelanoma skin cancer and others), major adverse cardiovascular events, and venous thromboembolism.

Conclusions: In abrocitinib trials, proportions of patients reporting any AE were generally consistent across age groups. However, compared with other age groups, patients ≥65 years of age were more likely to experience serious or severe AEs and several safety events of interest. Overall, these findings suggest that patients ≥65 years of age may require closer monitoring during abrocitinib treatment.

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6. Efficacy of Abrocitinib in Patients With Severe and Difficult-to-Treat Atopic Dermatitis in the Phase 3 JADE COMPARE Study

Jonathan Silverberg,[1] Eric Simpson,[2] Jacob P. Thyssen,[3] Manuelle Viguier,[4] Diamant Thaçi,[5] Marjolein de Bruin-Weller,[6] Stephan Weidinger,[7] Gary Chan,[8] Marco DiBonaventura,[9] Pinaki Biswas,[9] Claire Feeney,[10] Christoforos Koulias[11]

[1]The George Washington University School of Medicine and

Health Sciences, Washington, DC, USA; [2]Oregon Health & Science University, Portland, OR, USA; [3]Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark; [4]Centre Hospitalier Universitaire de Reims, Reims, France; [5]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany; [6]University Medical Center Utrecht, Utrecht, Netherlands; [7]University Hospital Schleswig-Holstein, Kiel, Germany; [8]Pfizer Inc., Collegeville, PA, USA; [9]Pfizer Inc., New York, NY, USA; [10]Pfizer Ltd., Tadworth, Surrey, United Kingdom; [11]Pfizer Hellas S.A., Athens, Greece

Introduction: Abrocitinib is an oral, once-daily, Janus kinase 1-selective inhibitor, under investigation for the treatment of moderate-to-severe atopic dermatitis (AD). Patients with moderate-to-severe AD, particularly those with severe AD that is refractory to other systemic therapies, experience substantial burden and unmet needs. We assessed the efficacy of abrocitinib in patients with severe and difficult-to-treat AD in the phase 3 study JADE COMPARE (NCT03720470).

Methods: Adults with moderate-to-severe AD received background medicated topical therapy plus once-daily oral abrocitinib 200 mg or 100 mg, dupilumab 300 mg subcutaneous injection every 2 weeks (after a 600-mg loading dose), or placebo. Severe and difficult-to-treat AD at baseline was defined based on the following criteria: (1) Investigator's Global Assessment (IGA) score of 4; (2) previous treatment of AD with any systemic immunosuppressant, including corticosteroids; and (3) body surface area (%BSA) involvement >50%. Efficacy was defined as achievement of an IGA response of clear (0) or almost clear (1) and improvement of ≥2 grades from baseline and ≥75% improvement from baseline in the Eczema Area and Severity Index (EASI-75) at week 12.

Results: At week 12, among patients with baseline IGA=4 (n=293), significantly higher IGA response rates were achieved with abrocitinib 200 mg and 100 mg than with placebo (49% and 25% vs 2%) and with abrocitinib 200 mg compared with dupilumab (49% vs 25%). Similar differences in IGA response at week 12 were observed among patients who had previously received systemic therapy (n=355) (abrocitinib 200 mg, 54%; abrocitinib 100 mg, 38%; placebo, 11%; dupilumab, 37%) and those with %BSA >50% (n=354) (abrocitinib 200 mg, 53%; abrocitinib 100 mg, 28%; placebo, 9%; dupilumab, 30%). Analysis of EASI-75 response rates revealed a similar pattern across all 3 severe and difficult-to-treat AD subgroups.

Conclusion: Abrocitinib 200 mg plus background medicated topical therapy was particularly effective relative to placebo and dupilumab in improving signs in patients with severe and difficult-to-treat AD.

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7. Efficacy of Abrocitinib Monotherapy for the Treatment of Moderate-to-Severe Atopic Dermatitis by Race

Andrew F. Alexis,[1] Jonathan I. Silverberg,[2] Zakiya P. Rice,[3] April W. Armstrong,[4] Seemal R. Desai,[5,6] Luz Fonacier,[7] Kenji Kabashima,[8] Mark Levenberg,[9] Pinaki Biswas,[9] Ricardo Rojo Cella,[10] Gary L. Chan[10]

[1]Weill Cornell Medical College, New York, NY, USA; [2]The George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [3]Dermatology Associates of Georgia, Atlanta, GA, USA; [4]Keck School of Medicine of University of Southern California, Los Angeles, CA, USA; [5]Innovative Dermatology, Plano, TX, USA; [6]University of Texas Southwestern Medical Center, Dallas, TX, USA; [7]NYU Langone Hospital–Long Island, Mineola, NY, USA; [8]Kyoto University, Kyoto, Japan; [9]Pfizer Inc., New York, NY, USA; [10]Pfizer Inc., Groton, CT, USA

Introduction: Racial/ethnic differences in prevalence, clinical manifestations, and health care utilization rates among US atopic dermatitis (AD) patients have been reported. In this post hoc analysis of clinical trial data, we assessed the efficacy of abrocitinib, a Janus kinase 1–selective inhibitor, by self-identified racial category (race).

Methods: We pooled data by self-reported race from phase 3 studies NCT03349060 and NCT03575871 and a phase 2b study NCT02780167. Participants with moderate-to-severe AD aged ≥12 years (phase 3) or ≥18 years (phase 2) were randomly assigned to abrocitinib 200 mg, abrocitinib 100 mg, or placebo once daily for 12 weeks. Endpoints included Investigator's Global Assessment (IGA) response (clear [0] or almost clear [1] with ≥2 grade improvement) and ≥75% improvement in Eczema Area and Severity Index (EASI-75). Statistical comparisons were based on the Cochran-Mantel-Haenszel test.

Results: Abrocitinib 200 mg, abrocitinib 100 mg, and placebo were administered, respectively, to 232, 254, and 142 White patients; 85, 80, and 39 Asian patients; and 30, 31, and 22 Black patients. At week 12, IGA response was significantly greater with abrocitinib 200 mg or 100 mg vs placebo in White (43% and 24% vs 9%), Asian (38% and 30% vs 10%), and Black (28% and 36% vs 0%) patients. Per EASI-75, a significant treatment effect was observed in White (64% and 39% vs 12%) and Asian (61% and 48% vs 13%) patients. In Black patients, the treatment effect with abrocitinib 100 mg (48%), but not 200 mg (38%), was statistically greater than placebo (14%). Adverse events with abrocitinib 200 mg and 100 mg were more common in White (75% and 70%; placebo, 61%) and Black patients (67% and 74%; placebo, 46%) than in Asian patients (65% and 59%; placebo, 41%). A similar pattern was observed with study discontinuation except that discontinuation was more common with placebo, regardless of race, presumably because of uncontrolled AD.

Conclusions: In this post hoc analysis, abrocitinib monotherapy (200 mg or 100 mg) was more efficacious than placebo in improving moderate-to-severe AD regardless of patient race.

Adverse events were more common in White and Black patients than in Asian patients. Lower efficacy and absence of dose response in Black patients might be an artifact of small sample size. Greater representation of Black patients in clinical studies is warranted.

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8. Outcomes in Patients With Atopic Dermatitis and Asthma: Analysis From the JADE REGIMEN Trial

Eric Simpson,[1] Jonathan Silverberg,[2] Jacek Zdybski,[3] Michael J. Cork,[4] Carle Paul,[5] Claire Feeney,[6] Claire Clibborn,[6] Marco DiBonaventura,[7] Pinaki Biswas,[7] Erman Guler[8]

[1]Oregon Health & Science University, Portland, OR, USA; [2]The George Washington University School of Medicine and Health Sciences, Washington DC, USA; [3]Dermedic Jacek Zdybski, Ostrowiec Świętokrzyski, Poland; [4]Sheffield Dermatology Research, University of Sheffield, Sheffield, United Kingdom; [5]Toulouse University and CHU, Toulouse, France; [6]Pfizer Ltd., Surrey, United Kingdom; [7]Pfizer Inc., New York, NY, USA; [8]Pfizer Inc., Istanbul, Turkey

Introduction: Asthma is common in patients with moderate-to-severe atopic dermatitis (AD). Janus kinase 1 (JAK1) inhibition reduces inflammation in AD, but its effects on asthma are not known. The JADE REGIMEN study (NCT03627767) evaluated response to 12 weeks of open-label induction (OLI) with the JAK1 inhibitor abrocitinib 200 mg in participants with moderate-to-severe AD, as well as long-term maintenance of that response with continuous or reduced (100 mg) abrocitinib dosing or placebo. In this post hoc analysis, we assessed AD and asthma outcomes in participants with asthma treated in the OLI phase.

Methods: Study NCT03627767 included patients (≥12 years) with moderate-to-severe AD. We analyzed the following data from participants with asthma at baseline: Investigator's Global Assessment [IGA] score of 0/1 with ≥2-grade improvement, 75% improvement in Eczema Area and Severity Index [EASI-75], ≥4-point improvement in Peak Pruritus Numerical Rating Scale (PP-NRS4; ©Regeneron Pharmaceuticals, Inc. and Sanofi (2017)).), Asthma Control Questionnaire-5 (ACQ-5) scores (on a scale of 0-6, where 0 is excellent control and 6 is extremely poor control), ≥4-point improvement in Dermatology Life Quality Index (DLQI-4), and safety.

Results: Of 1233 participants treated in the OLI phase, 403 (33%) had treatment-controlled asthma at baseline and were included in the analysis. Most participants were male (57%), white (77%), and had moderate AD (IGA=3; 55%). Median baseline ACQ score was 0.8 (Q1/Q3 0.2-1.6). At week 12, the proportion of participants with asthma who achieved IGA 0/1 was 59%; EASI-75, 72%; IGA 0/1 and EASI-75, 58%; and PP-NRS4, 67%. These response rates were comparable to those observed in the overall study. At the end of OLI, median ACQ score was 0.4 (Q1/Q3 0.0-1.0). The proportion of participants with asthma who achieved DLQI-4 between weeks 2 and 12 ranged from 84% to 91%. During the OLI period, 70% of participants reported adverse events (AEs), and 3% reported severe AEs. Overall, 6 participants (1.5%) reported asthma as a mild or moderate AE (3 each) and 3 participants (0.7%) reported asthmatic crisis. The safety profile was consistent with that of the overall study population.

Conclusion: Overall, AD outcomes after 12 weeks of once-daily abrocitinib 200 mg in participants with moderate-to-severe AD with concomitant asthma were similar to those of the overall study population in JADE REGIMEN. Abrocitinib did not significantly improve ACQ scores in this study, but a numerical trend toward improvement was observed.

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9. A Randomized, Double-blind, Vehicle-controlled Phase 2a Study Evaluating Once Daily Roflumilast Foam 0.3% in Patients With Moderate to Severe Seborrheic Dermatitis

Matthew Zirwas; on behalf of the Roflumilast Study 203 investigators and authors

Dermatologists of the Central States, Probity Medical Research, and Ohio University, OH, USA

Introduction: Seborrheic dermatitis (SD) is a chronic, inflammatory condition with scaling, erythematous, hyperpigmented, or hypopigmented patches on the scalp, face, upper trunk, and intertriginous areas. Affected individuals may experience itching, stress, or low self-esteem and need effective, well-tolerated treatments that are safe for chronic use on scalp and non-scalp locations. Topical roflumilast is a selective, highly potent phosphodiesterase-4 inhibitor. Here, we report results from a phase 2, 8-week, vehicle-controlled, double-blind study evaluating safety and efficacy of once-daily roflumilast foam 0.3% in patients with moderate or severe SD (NCT04091646).

Methods: Participants (≥18 years) with SD involving ≤20% body surface area (BSA; scalp and/or rest of body) and moderate or severe disease severity (Investigator Global Assessment [IGA] score 3–4) were randomized 2:1 to once-daily roflumilast 0.3% or vehicle foam (maximum application area ≤20% BSA) for 8 weeks.

Results: A total of 226 patients were randomized (roflumilast: n=154; vehicle: n=72). Baseline disease characteristics were comparable between groups. The primary efficacy endpoint, IGA Success (Clear/Almost Clear plus ≥2-grade improvement) at Week 8, was achieved by 73.8% and 40.9% of the roflumilast and vehicle foam groups, respectively (P<0.0001); 35.5% and 15.2%, respectively, were clear (IGA=0). Significant efficacy with roflumilast foam 0.3% was observed for numerous secondary endpoints, including IGA Success at Week 2 (33.8% vs 14.7%; P=0.0033) and Week 4 (56.6% vs 28.4%; P=0.0002); erythema success at Week 8 (44.7% vs 21.2%; P=0.0021); scaling success at Week 8 (56.0% vs 27.3%; P=0.0003); and, among patients with baseline Worst Itch Numeric Rating Scale (WI-NRS) ≥4 (n=184/226 [81.4%]), WI-NRS success (≥4-point improvement) at Week 2 (52.8% vs 23.2%; P=0.0007) and Week 8 (64.6% vs 34.0%; P=0.0007). The treatment benefit of roflumilast over vehicle was also supported by change from baseline in BSA at Week 8 (P<0.0001) and improvement in Dermatology Life Quality Index (P=0.0380 at Week 8.) Excellent tolerability was observed for roflumilast foam 0.3% with ≥98% of patients rated as having "no evidence of irritation" by the investigator. Overall incidence of treatment-emergent adverse events (TEAE) and TEAEs leading to discontinuation were low with similar rates between roflumilast and vehicle; no serious AEs were reported.

Conclusions: Once-daily roflumilast foam 0.3% significantly improved disease severity, erythema, scaling, and quality of life, itch with onset of action as early as Week 2 (first post-baseline visit). Roflumilast foam 0.3% was well-tolerated with low rates of AEs, supporting further study of roflumilast foam 0.3% as a promising treatment option for patients with moderate or severe SD.

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10. Once-Daily Roflumilast Cream 0.3%, a Potent Phosphodiesterase-4 Inhibitor, Provided Safe and Effective Treatment of Psoriasis in the DERMIS-1 and DERMIS-2 Phase 3 Trials

Mark Lebwohl; on behalf of the DERMIS-1 and DERMIS-2 investigators and authors

Icahn School of Medicine at Mount Sinai, NY, USA

Introduction: Roflumilast cream 0.3%, a selective and highly potent phosphodiesterase-4 inhibitor, is a highly effective, well-tolerated, nonsteroidal, once-daily treatment for long-term management of psoriasis. We describe the effects of once-daily roflumilast cream 0.3% on plaque psoriasis during two Phase 3, randomized, double-blind, vehicle-controlled, multi-center trials.

Methods: DERMIS-1 (N=439; NCT04211363) and DERMIS-2 (N=442; NCT04211389) were identical Phase 3 trials conducted in patients (≥2 years) with psoriasis involving 2-20% of body surface area (BSA). Patients were randomized 2:1 to once-daily roflumilast cream 0.3% or vehicle for 8 weeks. The primary efficacy endpoint was Investigator Global Assessment (IGA) Success (IGA status of Clear or Almost Clear plus ≥2-grade improvement from baseline) at Week 8.

Results: In both studies, significantly more roflumilast-treated patients than vehicle-treated patients achieved IGA Success (DERMIS-1: 42.4% vs. 6.1%; DERMIS-2: 37.5% vs 6.9%, P<0.001 for both) at Week 8. Statistically significant differences favoring roflumilast were observed for multiple secondary endpoints, including percentage of patients achieving intertriginous-IGA Success (DERMIS-1: 71.2% vs. 13.8%; DERMIS-2: 68.1% vs. 18.5%, P<0.01), percentage of patients achieving 75% reduction in Psoriasis Area Severity Index (DERMIS-1: 41.6% vs. 7.6%; DERMIS-2: 39.0% vs 5.3%, P<0.0001), percentage of patients achieving 90% reduction in Psoriasis Area Severity Index (DERMIS-1: 22.4% vs. 2.3%; DERMIS-2: 17.0% vs 2.3%, P<0.0001), and percentage of patients with baseline Worst Itch-Numeric Rating Scale ≥4 achieving a 4-point reduction in WI-NRS (DERMIS-1: 67.5% vs 26.8%; DERMIS-2: 69.4% vs 35.6%, P<0.0001) at week 8. Roflumilast also demonstrated superior improvement from baseline in BSA compared with vehicle at Weeks 2-8 (P≤0.01). The improvements in investigator-assessed disease severity were consistent with improvements in patient-reported disease severity and burden as indicated by a significantly greater reduction in total Psoriasis Symptom Diary score compared with vehicle-treated patients. At Week 8, least square mean difference in percentage change from baseline total PSD score compared with vehicle treatment was -54.3% in DERMIS-1 and -38.8% in DERMIS-2 (P<0.001). Local tolerability was highly favorable as reported by patient and investigator assessment of irritation, burning, and stinging. On investigator-rated local tolerability, over 96% of patients in each group had no evidence of irritation at Week 4 or Week 8. On patient-rated local tolerability, scores were low (favorable) and similar to vehicle at all timepoints. Overall incidence of treatment-emergent adverse events (TEAE), serious adverse events, and TEAEs leading to discontinuation were low with similar rates between roflumilast and vehicle across both studies.

Conclusions: Roflumilast cream 0.3% provided superior improvement across multiple efficacy endpoints versus vehicle cream while demonstrating onset as early as 2 weeks with favorable safety and tolerability in patients with psoriasis in two Phase 3 trials.

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11. Once-daily Roflumilast Foam 0.3% Improves Severity and Burden of Itch in Patients With Scalp and Body Psoriasis in a Randomized, Double-blind, Vehicle-controlled Phase 2b Study

Angela Y. Moore; on behalf of the Roflumilast Study 204 investigators and authors

Arlington Center for Dermatology, Arlington Research Center, TX, USA

Introduction: Psoriasis frequently affects the scalp – a difficult-to-treat area with potentially greater impact on quality of life (QoL) than other areas. Many patients favor foam formulations for treating hair-bearing areas. Roflumilast is a selective and highly potent inhibitor of phosphodiesterase-4 being evaluated as a non-steroidal topical treatment for inflammatory skin disorders. A phase 2b, double-blind, vehicle-controlled 8-week study evaluated efficacy and safety of roflumilast 0.3% foam in patients with scalp and body psoriasis (NCT04128007). The study met its primary endpoint of Investigator Global Assessment of Scalp (S–IGA) Success (Clear/Almost Clear status plus ≥2-grade reduction from baseline) at Week 8, achieved by 59.1% of patients receiving roflumilast versus 11.4% receiving vehicle (P<0.0001). Significant improvement was also observed for Investigator Global Assessment of Body (B-IGA) success at week 8 (40.3% with roflumilast vs. 6.8% with vehicle; P<0.0001). Significantly greater success on S-IGA and B-IGA were observed as early as 2 weeks (P≤0.0008 and P≤0.0082, respectively). Here we describe effects of once-daily roflumilast foam on itch in patients with scalp and body psoriasis.

Methods: Patients (≥12 years) with at least mild disease (S–IGA ≥2 and B–IGA ≥2) were randomized 2:1 to once-daily roflumilast 0.3% or vehicle foam. Safety and efficacy were evaluated at Weeks 2, 4, and 8. Secondary and exploratory endpoints included Scalp Itch–Numeric Rating Scale (SI–NRS), Worst Itch–Numeric Rating Scale (WI–NRS), Psoriasis Symptoms Diary (PSD), and Dermatology Life Quality Index (DLQI).

Results: Overall 304 patients were randomized (roflumilast 0.3%: n=200; vehicle foam: n=104); 302 completed Week

8 disease assessments. Baseline disease characteristics were comparable between groups. Among patients with baseline SI–NRS score ≥4 (n=269/304 [88.5%]), SI–NRS success (≥4-point reduction from baseline) was achieved by significantly higher percentages of roflumilast-treated patients versus vehicle-treated patients (P<0.0001 for all timepoints). Among patients with baseline WI–NRS score ≥4 (n=259/304 [85.2%]), WI–NRS success (≥4-point reduction from baseline) was achieved by significantly higher percentages of the roflumilast group (P<0.0001 at all timepoints). Severity and burden of itch were reduced more with roflumilast than with vehicle as indicated by mean percentage change from baseline scores in PSD items 1 and 2, respectively (P-values not calculated). Roflumilast provided greater overall QoL benefit with greater absolute mean percentage change from baseline in DLQI total scores (P<0.0001 for all timepoints). Rates of treatment-related adverse events (AEs) and AEs leading to discontinuation were low and comparable between groups.

Conclusions: Once-daily roflumilast foam 0.3% provided significant and consistent efficacy versus vehicle across several measurements of itch with onset of action by 2 weeks and improved QoL. Roflumilast foam represents a novel, effective, and well-tolerated non-steroidal topical treatment of scalp and body psoriasis.

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12. Roflumilast Cream 0.3% Improved the Severity and Impact of Itch in Patients With Chronic Plaque Psoriasis in the Phase 3 DERMIS-1 and DERMIS-2 Studies

Melinda J. Gooderham; on behalf of the DERMIS-1 and DERMIS 2 investigators and authors

SkiN Centre for Dermatology/Probity Medical Research/ Queen's University, ON, Canada

Introduction: Roflumilast is a selective and highly potent phosphodiesterase-4 inhibitor being investigated as a non-steroidal topical treatment for inflammatory skin diseases. Once-daily roflumilast cream 0.3% demonstrated favorable safety and tolerability while delivering statistically superior efficacy vs. vehicle in patients with chronic plaque psoriasis from two phase 3 trials, DERMIS-1 (NCT04211363) and DERMIS-2 (NCT04211389). Both studies met the primary endpoint of Investigator Global Assessment (IGA) success (Clear/Almost Clear plus ≥2-grade improvement from baseline) at Week 8 with roflumilast compared with vehicle (DERMIS-1: 42.4% vs 6.1%, P<0.0001; DERMIS-2: 37.5% vs 6.9%, P<0.0001). Here we report patient-reported outcomes, including itch, the most burdensome and frequently reported symptom associated with psoriasis.

Methods: Two identical phase 3, double-blind trials randomized patients (≥2 years) with psoriasis 2:1 to once-daily roflumilast cream 0.3% or vehicle cream for 8 weeks. Secondary patient-reported endpoints included ≥4-point improvement in Worst Itch-Numeric Rating Scale (WI–NRS) score at Week 8 in patients with baseline WI–NRS score ≥4 and change from baseline on Items 1 (severity of itch) and 2 (burden of itch) Psoriasis Symptoms Diary (PSD) scores. Quality of life (QoL) was measured using the Dermatology Life Quality Index (DLQI) at Weeks 2, 4, and 8. For all 3 instruments, lower scores indicate better outcomes.

Results: In DERMIS-1, 439 patients were randomized (roflumilast 0.3%: n=286; vehicle: n=153) and 442 patients were randomized (roflumilast 0.3%: n=290; vehicle: n=152) in DERMIS-2. Baseline disease characteristics were comparable across treatment groups and studies. Across both studies, least square mean change from baseline in WI–NRS score was significantly greater with roflumilast than with vehicle at all timepoints (all P<0.0001) with improvement as early as 2 weeks. Among patients with baseline WI–NRS score ≥4 (DERMIS-1: n=333/439 [75.9%]; DERMIS-2: n=345/442 [78.1%]), percentages of patients achieving ≥4-point reduction were significantly greater with roflumilast than with vehicle at Weeks 4, 6, and 8 in DERMIS-1 (P<0.0001) and at all timepoints in DERMIS-2 (P≤0.0026). Significantly greater changes from baseline in severity and burden of itch were observed with roflumilast versus vehicle from Weeks 2 to 8. The change from baseline in DLQI total scores also favored roflumilast over vehicle at the 3 timepoints evaluated (P≤0.0002). Overall incidence of treatment-emergent adverse events (TEAE), serious adverse events, and TEAEs leading to discontinuation were low with similar rates between roflumilast and vehicle across both studies.

Conclusions: Once-daily roflumilast cream 0.3% provided significant, consistent, and sustained improvements in the severity and burden of itch and QoL compared with vehicle in patients with psoriasis. These studies support the potential use of roflumilast as an effective and well-tolerated non-steroidal topical therapy for improving patient burden and QoL in patients with psoriasis.

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13. Deucravacitinib, a Selective Tyrosine Kinase 2 (TYK2) Inhibitor: Overview of Clinical Pharmacology Including ADME, Food and pH Effects, Pharmacokinetics in Special Populations, and Drug-Drug Interactions

Anjaneya Chimalakonda, Shalabh Singhal, Randy Dockens, Miroslawa Nowak, David Marchisin, Ihab G. Girgis, Subhashis Banerjee, John Throup, Urvi Aras, Wenying Li, Bindu Murthy

Bristol Myers Squibb, Princeton, NJ, USA

Introduction: TYK2 mediates signaling by interleukin (IL)-23, IL-12, and Type I interferons, which are involved in the pathogenesis of psoriasis and other immune-mediated disorders. Deucravacitinib is an oral, selective inhibitor of TYK2 with high functional selectivity for this kinase compared with other TYK inhibitors, including Janus kinases 1/2/3. Deucravacitinib achieves high selectivity by binding to the regulatory domain, unlike other kinase inhibitors, which bind to the structurally conserved ATP-binding site in the kinase domain. Two pivotal Phase 3 trials in plaque psoriasis, POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751), demonstrated superiority

for deucravacitinib versus placebo and apremilast. Here, we summarize key pharmacologic properties of deucravacitinib, including absorption, distribution, metabolism, and excretion (ADME), food effects, pH effects, pharmacokinetics (PK) in special populations, and drug-drug interactions (DDIs).

Methods: The PK/ADME profile of deucravacitinib integrated in vitro and in vivo data. Exposure and ADME characteristics were analyzed in single- and multiple-ascending dose studies and in a mass balance study. Dedicated studies evaluated food effects, pH effects, PK in renal and hepatic-impaired subjects, and DDIs (including medications commonly used in inflammatory diseases) on maximum observed concentration (Cmax) and area under the curve (AUC) of deucravacitinib.

Results: PK/ADME analyses demonstrated oral deucravacitinib is rapidly absorbed and subsequently eliminated by multiple well-balanced metabolic and elimination pathways, including renal elimination. Deucravacitinib does not meaningfully induce or inhibit common cytochrome P450 or uridine 5'-diphospho-glucuronosyltransferase enzymes or drug transporters. Gastric pH modulators (famotidine, rabeprazole) and food had minor effects on deucravacitinib Cmax (<30%) and AUC (<11%). Cmax (max. change, ≤1.1-fold) and AUC (max. change, ≤1.6-fold) were modestly affected in patients with mild, moderate, or severe renal impairment and with mild or moderate hepatic impairment. Concomitant cyclosporine, fluvoxamine, ritonavir, pyrimethamine, and diflunisal had minor effects on deucravacitinib Cmax (max. change, <1.2-fold) and AUC (max. change, <1.6-fold). Deucravacitinib had negligible effects on the Cmax and AUC of rosuvastatin (≤15%), oral contraceptives (≤10%), methotrexate (≤11%), and mycophenolate mofetil (≤8% based on major active species [mycophenolic acid]). Effects on drug exposures were not considered clinically meaningful.

Conclusion: Deucravacitinib exhibited favorable PK/ADME profiles; its exposures were not meaningfully influenced by multiple concomitant medications. Deucravacitinib did not meaningfully alter exposure of relevant medications, including oral contraceptives and common medications used in psoriatic disease. This suggests deucravacitinib can be administered regardless of food consumption to patients with any level of renal or mild-moderate hepatic impairment, and along with relevant concomitant medications.

Disclosures: AC, SS, RD, MN, DM, IGG, SB, JT, UA, WL, and **BM:** Employees and shareholders: Bristol Myers Squibb.

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14. Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor Versus Placebo and Apremilast in Moderate to Severe Plaque Psoriasis: Efficacy Analysis by Baseline Disease Characteristics From the Phase 3 POETYK PSO-1 and PSO-2 Trials

Joseph F. Merola,[1] Howard Sofen,[2] Diamant Thaçi,[3] Carle Paul,[4] Shinichi Imafuku,[5] Subhashis Banerjee,[6] Elizabeth Colston,[6] Jonghyeon Kim,[6] John Throup,[6] April W. Armstrong[7]

[1]Brigham and Women's Hospital, Brigham Dermatology Associates, Harvard Medical School, Boston, MA, USA; [2]UCLA School of Medicine, Los Angeles, CA, USA; [3]University of Lübeck, Lübeck, Germany; [4]Larrey University Hospital, Paul Sabatier University, Toulouse, France; [5]Fukuoka University Hospital, Fukuoka, Japan; [6]Bristol Myers Squibb, Princeton, NJ, USA; [7]University of Southern California, Los Angeles, CA, USA

Introduction: Deucravacitinib is a highly selective TYK2 inhibitor that mediates signaling of key cytokines in psoriasis pathogenesis. In the POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) Phase 3 trials, significantly greater proportions of patients achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) score and static Physician's Global Assessment (sPGA) score of 0/1 with deucravacitinib versus placebo and apremilast. This analysis evaluated responses by prespecified baseline disease characteristics.

Methods: Adults with moderate to severe plaque psoriasis were randomized 1:2:1 to placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily. Coprimary endpoints were the proportions of patients achieving PASI 75 and sPGA 0/1 responses versus placebo at Week 16. Subgroup analyses were performed for coprimary endpoints versus placebo or apremilast at Week 16 across prespecified baseline characteristics (moderate versus severe disease sPGA 3, 4; PASI 12–20, >20; body surface area [BSA] 10%–20%, >20%), disease duration (<10 y, ≥10 y), and age at disease onset (<18 y, 18–39 y, ≥40 y).

Results: 666 and 1020 patients were randomized in PSO-1 and PSO-2, respectively. Baseline disease characteristics were balanced across the trials and treatment groups and represented a population with moderate to severe plaque psoriasis. Proportions of patients with moderate psoriasis in PSO-1 and PSO 2, respectively, were 78.7% and 80.5% (baseline sPGA 3), 56.6% and 58.1% (baseline PASI 12–20), and 51.5% and 49.4% (baseline BSA 10%–20%). Median (range) PASI at baseline was 19.0 (10.3–58.8) (PSO-1) and 18.6 (12.0–66.8) (PSO-2). Median (range) disease duration was 14.5 (0.7–62.3) y (PSO-1) and 17.6 (0.6–67.5) y (PSO-2). Significantly higher responses were achieved with deucravacitinib at Week 16 versus placebo and apremilast based on PASI 75 (PSO-1: 58.7% vs 12.7% and 35.1%, P<0.0001 [both]; PSO-2: 53.6% vs 9.4% and 40.2%, P≤0.0003 [both]) and sPGA 0/1 (PSO-1: 53.6% vs 7.2% and 32.1%, P<0.0001 [both]; PSO-2: 50.3% vs 8.6% and 34.3%, P<0.0001 [both]). Greater efficacy versus placebo and apremilast at Week 16 was observed for most outcomes regardless of baseline disease severity, disease duration, and age of disease onset.

Conclusion: PASI 75 and sPGA 0/1 responses were superior with deucravacitinib versus placebo and apremilast across nearly all prespecified baseline disease parameters, including measures of disease severity and duration of psoriasis.

Disclosures: JFM: Consultant and/or investigator: Amgen, AbbVie, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB

HS: Clinical investigator: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis, and Sun Pharma

DT: Advisory board, principal investigator, and lecture fees: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DS Pharma, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche-Posay, Samsung, Sandoz-Hexal, Sanofi, and UCB

CP: Grants and consulting: Almirall, Amgen, AbbVie, Bristol Myers Squibb, Boehringer, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Mylan, Novartis, Pfizer, Pierre Fabre, Sanofi, and UCB

SI: Grants and personal fees: AbbVie, Eisai, Kyowa Kirin, Taiho Yakuhin, Maruho, Tanabe Mitsubishi, Leo Pharma, Janssen, Sun Pharma, and Torii Yakuhin; Personal fees: Amgen, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, Novartis, and UCB

SB, EC, JK, JT: Employees and shareholders: Bristol Myers Squibb

AWA: Grants and personal fees: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Parexel, Dermavant, Genentech, GlaxoSmithKline, Menlo Therapeutics, Merck, Modernizing Medicine, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Science 37, Sun Pharma, and Valeant; Grants: Dermira, Kyowa Hakko Kirin, and UCB, outside the submitted work

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

Diamant Thaçi,[1] Kenneth Gordon,[2] Melinda Gooderham,[3] Bruce Strober,[4] Neil J Korman,[5] Subhashis Banerjee,[6] Elizabeth Colston,[6] Jonghyeon Kim,[6] John Throup,[6] Akimichi Morita[7]

[1]University of Lübeck, Lübeck, Germany; [2]Medical College of Wisconsin, Milwaukee, WI, USA; [3]Probity Medical Research, Waterloo, ON, Canada; [4]Yale University, New Haven, CT, and Central Connecticut Dermatology, Cromwell, CT, USA; [5]Case Western Reserve University and University Hospitals, Cleveland, OH, USA; [6]Bristol Myers Squibb, Princeton, NJ, USA; [7]Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Introduction: Deucravacitinib, a novel, oral, selective TYK2 inhibitor, binds to the regulatory domain and inhibits TYK2 via an allosteric mechanism distinct from Janus kinase inhibitors that bind to the conserved active site in the kinase domain. In the Phase 3 POETYK PSO-1 and PSO-2 trials, deucravacitinib was significantly more efficacious than placebo or apremilast and well tolerated in patients with moderate to severe plaque psoriasis. This analysis used integrated data from both trials to compare the effects of deucravacitinib versus placebo and apremilast on laboratory parameters.

Methods: The double-blind, 52-week POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) trials randomized patients with moderate to severe plaque psoriasis (body surface area ≥10%, Psoriasis Area and Severity Index [PASI] ≥12, static Physician's Global Assessment ≥3) 1:2:1 to placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily. Patients receiving placebo were switched to deucravacitinib at Week 16; patients receiving apremilast who failed to meet trial-specific efficacy thresholds (PSO-1: PASI 50; PSO-2: PASI 75) were switched to deucravacitinib at Week 24. Changes from baseline levels of lymphocytes, neutrophils, platelets, hemoglobin, total cholesterol, triglycerides, creatine phosphokinase (CPK), creatinine, ALT, and AST were evaluated. Shifts in CTCAE (v5.0) severity grade of laboratory parameter abnormalities between baseline and Week 16 were assessed. Integrated data from PSO-1 and PSO-2 are presented.

Results: In total, 666 and 1020 patients were randomized in PSO-1 and PSO-2, respectively, and included in this analysis. Overall, no clinically meaningful changes from baseline levels were observed in any laboratory parameter over the placebo-controlled period (Weeks 0–16). Grade ≥3 laboratory abnormalities occurred at low frequencies and were comparable across treatment groups through Week 16; shifts of ≥2 CTCAE grades from baseline were balanced overall and infrequent in all treatment groups. Triglyceride and CPK elevations were low and similar across treatment arms (<1.8%). No clinically relevant cumulative trends in laboratory parameters were observed up to Week 52 in patients randomized to deucravacitinib at baseline in PSO-1 who continued to receive deucravacitinib over 52 weeks.

Conclusion: Deucravacitinib did not result in clinically significant laboratory parameter abnormalities in 2 large Phase 3 trials in psoriasis, suggesting routine laboratory monitoring during deucravacitinib treatment may not be warranted.

Disclosures: DT: Advisory board, principal investigator, and lecture fees: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DS Pharma, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche-Posay, Samsung, Sandoz-Hexal, Sanofi, and UCB

KG: Grant support and consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and UCB; Consulting fees: Amgen, Almirall, Dermira, Leo Pharma, Pfizer, and Sun Pharma

MG: Advisory board, principal investigator, and lecture fees: AbbVie, Galderma, Leo Pharma, Pfizer, and Regeneron; Advisory board and lecture fees: Actelion Pharmaceuticals; Principal investigator and consulting fees: Akros Pharma; Advisory board, principal investigator, lecture fees, and consulting fees: Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Novartis, Sanofi Genzyme, Valeant; Principal investigator: Arcutis, Bristol Myers Squibb, Dermira, GlaxoSmithKline, MedImmune, Merck, Roche Laboratories, and UCB; Principal investigator and lecture fees: Glenmark

BS: Honoraria or consultation fees: AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Immunic Therapeutics, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, Equillium,

Janssen, Leo Pharma, Maruho, Meiji Seika Pharma, Mindera, Novartis, Pfizer, GlaxoSmithKline, Ortho Dermatologics, Regeneron, Sanofi Genzyme, Sun Pharma, UCB, and Ventyxbio; Speaker: AbbVie, Janssen, Lilly, and Sanofi Genzyme; Scientific co-director (consulting fee): CorEvitas' Psoriasis Registry; Investigator: AbbVie, Cara, CorEvitas' Psoriasis Registry, Dermavant, Eli Lilly/Dermira, and Novartis

NJK: Advisory board, consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Principia, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB; Grant support/principal investigator: AbbVie, Amgen, Argenx, Bristol Myers Squibb, Celgene, Chemocentryx, Eli Lilly, Galderma, Kyowa Hakko Kirin, Leo Pharma, Menlo, Principia, Prothena, Rhizen, Syntimmune, Trevi, and Xbiotech. Speaker: AbbVie, Eli Lilly, Janssen, Novartis, Regeneron, and Sanofi Genzyme

SB, EC, JK, and JT: Employees and shareholders: Bristol Myers Squibb.

AM: Grant/research support, consultant, speakers bureau: AbbVie, Boehringer Ingelheim,Bristol Myers Squibb, Celgene, Eli Lilly, Eisai, Janssen, Kyowa Hakko Kirin, Leo Pharma, Maruho, Mitsubishi Tanabe, Nichi-Iko, Nippon Kayaku, Novartis, Pfizer, Sun Pharma, Taiho Pharmaceutical, Torii Pharmaceutical, UCB, and Ushio

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16. Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, Versus Placebo and Apremilast in Moderate to Severe Plaque Psoriasis: Onset of Action in the Phase 3 POETYK PSO-1 and POETYK PSO-2 Trials

Neil J Korman,[1] Kim Papp,[2] Jerry Bagel,[3] Peter Foley,[4] Akimichi Morita,[5] Subhashis Banerjee,[6] Elizabeth Colston,[6] Tao Wang,[6] John Throup,[6] Diamant Thaçi[7]

[1]Case Western Reserve University and University Hospitals, Cleveland, OH, USA; [2]Probity Medical Research, Waterloo, ON, Canada; [3]Windsor Dermatology, East Windsor, NJ; [4]Skin Health Institute, Carlton, VIC, Australia; [5]Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; [6]Bristol Myers Squibb, Princeton, NJ, USA; [7]University of Lübeck, Lübeck, Germany

Introduction: TYK2 is an intracellular kinase that mediates signaling by key cytokines (interleukin [IL]-23, IL-12, and Type I interferons) in psoriasis pathogenesis. Deucravacitinib is a novel oral agent that selectively inhibits TYK2 via an allosteric mechanism by binding to the regulatory domain. In the Phase 3 POETYK PSO-1 and PSO-2 trials, deucravacitinib was significantly more efficacious than placebo or apremilast and was well tolerated in patients with psoriasis. This analysis compares the onset of action of deucravacitinib versus placebo and apremilast using data from PSO-1 and PSO-2.

Methods: PSO-1 (NCT03624127) and PSO-2 (NCT03611751) were double-blinded, 52-week trials that randomized patients with moderate to severe plaque psoriasis 2:1:1 to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily. Onset of action was evaluated as mean change from baseline, adjusted for baseline covariates, in continuous objective and patient-reported efficacy outcomes sensitive to change, including PASI, BSA, sPGA×BSA, Psoriasis Symptoms and Signs Diary (PSSD) symptom score, and DLQI at Weeks 1, 2, 4, 8, 12, 16, 20, and 24. The proportion of patients achieving sPGA 0/1 response was determined.

Results: 666 and 1020 patients were randomized in PSO-1 and PSO-2, respectively; baseline PASI, BSA, sPGA×BSA, PSSD symptom scores, and DLQI scores were similar across groups. Deucravacitinib treatment was associated with significantly larger adjusted mean changes from baseline in PASI versus placebo as early as Week 1 in both trials ($P<0.0001$). The proportion of patients achieving sPGA 0/1 response was significantly higher in the deucravacitinib group versus placebo by Week 4 ($P<0.0001$) and versus apremilast by Week 8 ($P\leq0.0018$). Similarly, deucravacitinib demonstrated significantly larger adjusted mean changes from baseline versus placebo in sPGA×BSA ($P\leq0.0052$) and DLQI ($P\leq0.025$) by Week 1 and in BSA ($P\leq0.0079$) and PSSD symptom score ($P\leq0.0002$) by Week 2. Significantly greater changes from baseline for deucravacitinib versus apremilast were seen in PSO-1 by Week 4 for PASI, BSA, and sPGAxBSA and by Week 8 for DLQI 0/1, and for all assessments by Week 8 in PSO-2. Deucravacitinib superiority was demonstrated to Week 16 versus placebo ($P<0.0001$) and to Week 24 versus apremilast ($P\leq0.0005$).

Conclusion: PSO-1 and PSO-2 demonstrated that oral deucravacitinib has a rapid onset of action and improves objective and patient-reported efficacy outcomes versus placebo as early as Week 1, and versus apremilast as early as Week 4. These findings suggest that deucravacitinib provides rapid sign and symptom relief in plaque psoriasis.

Disclosures: NJK: Advisory board, Consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Principia, Regeneron, Sanofi-Genzyme, Sun Pharma, UCB; Grant support/Principal investigator: AbbVie, Amgen, Argenx, Bristol Myers Squibb, Celgene, Chemocentryx, Eli Lilly, Galderma, Kyowa Hakko Kirin, Leo Pharma, Menlo, Principia, Prothena, Rhizen, Syntimmune, Trevi, Xbiotech; Speaker: AbbVie, Eli Lilly, Janssen, Novartis, Regeneron, Sanofi-Genzyme.

KP: Speakers bureau: AbbVie, Amgen, Astellas, Celgene, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Valeant; Grant/research support: AbbVie, Akros, Allergan, Amgen, Anacor, Arcutis, AstraZeneca, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Leo Pharma, MedImmune, Meiji Seika Pharma, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant; Consultant: AbbVie, Akros, Amgen, Arcutis, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, CanFite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Merck Serono, Merck Sharp & Dohme, Mitsubishi Pharma, Novartis, Pfizer, Regeneron,

Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant; Honoraria: AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Forward Pharma, Galderma, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Merck Serono, Merck Sharp & Dohme, Novartis, Pfizer, Takeda, UCB, Valeant; Scientific officer/Steering committee/Advisory board: AbbVie, Akros, Amgen, Anacor, Astellas, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Merck Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, Valeant.

JB: Research funds payable to the Psoriasis Treatment Center of New Jersey from AbbVie, Amgen, Arcutis Biotherapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corporation, CorEvitas' Psoriasis Registry, Dermavant Sciences, Dermira/UCB, Eli Lilly, Glenmark Pharmaceuticals, Janssen Biotech, Kadmon Corporation, Leo Pharma, Lycera Corp, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sun Pharma, Taro Pharmaceutical Industries, Valeant Pharmaceuticals; Consultant: AbbVie, Amgen, Celgene, Eli Lilly, Janssen Biotech, Novartis, Sun Pharma, Valeant Pharmaceuticals; Speaker: AbbVie, Celgene, Eli Lilly, Janssen Biotech, Novartis.

PF: Grant support: AbbVie, Amgen, Celgene, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Sanofi, Sun Pharma; Investigator: AbbVie, Amgen, AstraZeneca, Arcutis, Aslan, Boehringer Ingelheim, Botanix, Bristol Myers Squibb, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Galderma, Genentech, GSK, Hexima, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma, Valeant; Advisory board: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Galderma, GSK, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, Valeant; Consultant: Bristol Myers Squibb, Galderma, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Roche, UCB Pharma; Travel grants: AbbVie, Galderma, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Roche, Sun Pharma, Sanofi; Speaker for or honoraria from: AbbVie, Celgene, Galderma, GSK, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Roche, Valeant.

AM: Grant/research support, consultant, speakers bureau: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Eisai, Janssen, Kyowa Hakko Kirin, Leo Pharma, Maruho, Mitsubishi Tanabe, Nichi-Iko, Nippon Kayaku, Novartis, Pfizer, Sun Pharma, Taiho Pharmaceutical, Torii Pharmaceutical, Ushio, UCB Pharma

SB, EC, TW, JT: Employees and shareholders of Bristol Myers Squibb.

DT: Grant/research support, consultant, scientific advisory board, speakers bureau: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche, Sandoz-Hexal, Target-Solution, Sanofi, UCB.

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17. 31-Gene Expression Profiling with Clinicopathologic Features Improves Prognostication of Recurrence and Metastasisin Patients with Stage I-Iii Cutaneous Melanoma

Nicholas Taylor[1], Sebastian Podlipnik[2], Brian Martin[3], Ann Quick[3], Kyle Covington[3], Robert Cook[3]

[1]Zitelli and Brodland, P.C., Pittsburgh, PA, [2]Hospital Clinic of Barcelona, Barcelona, Spain, [3]Castle Biosciences, Inc., Friendswood, TX

Introduction: Patients with cutaneous melanoma (CM) are staged according to the American Joint Committee on Cancer (AJCC) criteria and receive melanoma-specific survival (MSS) estimates based on average cohort risk rather than personalized risk. Further, AJCC does not provide recurrence-free (RFS) or distant metastasis-free survival (DMFS) prognoses. The validated 31-gene expression profile (31-GEP) adds independent prognostic value to the current staging criteria.

Methods: An algorithm was developed (N=1581) and validated (N=523) using Cox regression on patients with stage I-III CM from multiple centers in the United States and Spain. Parameter selection was determined using 10x4-fold cross-validation. The final integrated algorithm (i31-GEP) combined the continuous 31-GEP score, Breslow thickness, ulceration, mitotic rate, sentinel lymph node status (SLN), tumor location, and age. The i31-GEP was compared to AJCC 8th edition using the net reclassification index (NRI).

Results: The 31-GEP score was an independent, significant predictor for RFS (HR 4.42, P<.001), DMFS (HR 3.36, P=.019), and MSS (HR 20.00, P=.002), as were Breslow thickness, tumor location (head and neck), and a positive SLN. Kaplan-Meier analysis showed i31-GEP predicted survival outcomes that aligned with observed outcomes, suggesting a well-calibrated algorithm. Compared to AJCC 8th edition, the i31-GEP significantly improved discrimination between the prediction of adverse event and non-events for 5-year RFS (NRI: 0.66, P=.001), DMFS (NRI: 0.73, P<.001), and MSS (NRI: 0.66, P<.001).

Conclusion: While the 31-GEP maintained independent value for survival prognostication, integrating the 31-GEP score with clinicopathologic features (i31-GEP) may help personalize patient management and risk prediction beyond standard melanoma staging.

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18. Clinical Utility of the 40-gene Expression Profile (40-GEP) for Improved Patient Management Decisions and Disease Related Outcomes when Combined with Current Clinicopathological Risk Factors for Cutaneous Squamous Cell Carcinoma (cSCC): Case Series

J Au, MD[1]; SJ Kurley, PhD[2]; A Fitzgerald, PhD[2]; A-K Somani, MD, PhD[1]

[1]Indiana University School of Medicine; [2]Castle Biosciences, Inc.

Introduction: While cutaneous squamous cell carcinoma (cSCC) has an overall favorable prognosis, a subset of patients will develop metastases and die from their disease. A prognostic 40-GEP test has recently been independently validated to improve stratification of

metastatic risk in high-risk cSCC patients. The 40-GEP test classifies patients into three groups based on risk for regional and/or distant metastasis (Class 1, low risk; Class 2A, moderate risk; Class 2B, high risk). National guidelines are unclear on which specific patients warrant additional management. Thus, treatment of high-risk cSCC often relies on risk assessment based on risk factors weighted by physician experience.

Study/Methods: Case 1 with a history of renal and liver transplantation and cSCC presented with a papule on his left temple that was previously treated with cryotherapy. It was diagnosed as a poorly differentiated cSCC (BWH* T2a, AJCC** stage T1). Mohs micrographic surgery (MMS) was completed in 4 stages and subsequent analysis of the last layer of non-marginal tissue was positive for cSCC. A review of the marginal frozen sections showed a small foci of cSCC. The patient was informed but declined further treatments. The patient was recurrence-free for 4 years (death due to unrelated causes) and retrospective analysis of the initial biopsy with the 40-GEP test provided a Class 1 result.

Case 2 with a history of liver transplantation and cSCC presented with a 2-month history of an exophytic growth on his left temple. It was diagnosed as a poorly differentiated cSCC (BWH T2a, AJCC stage T1) with subsequent removal with MMS in 2 stages 1 month later. Three months later, the patient noticed another growth immediately inferior to the linear scar line, as well as one on the ipsilateral helical root. The biopsy results were consistent with metastatic cSCC. Retrospective analysis of the initial biopsy with the 40-GEP test provided a Class 2B result.

Conclusions: We present two cases that highlight the utility of the 40-GEP test as an adjunct to enhance cSCC risk stratification. Each Case had the same initial BWH and AJCC staging, yet with distinctively different outcomes. Case 1 highlighted a biologically less aggressive tumor (with a retrospective 40-GEP Class 1 result) that did not recur despite incomplete surgical clearance. Case 2 highlighted a biologically aggressive tumor (with a retrospective 40-GEP Class 2B result) that developed regional metastasis despite clear surgical margins obtained through MMS. Adjuvant treatment might have been appropriate earlier in the disease course and may have altered his prognosis. Integrating novel molecular prognostication with traditional clinicopathological risk factors can improve stratification of high-risk cSCC patients and may inform selection of risk-appropriate treatment and surveillance strategies.

**BWH- Brigham and Women's Hospital staging*
**AJCC- American Joint Committee on Cancer*

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19. Integration of the 31-gene Expression Profile Test with Clinicopathologic Features (i31-GEP) to Assess Sentinel Lymph Node Positivity Risk in Patients with Cutaneous Melanoma

Eric Whitman[1], Ann Quick[2], Brian Martin[2], Christine Bailey[2], Kyle R. Covington[2], Robert Cook[2], David Hyams[3], John Vetto[4]

[1]Atlantic Health System Cancer Care, Morristown, NJ; [2]Castle Biosciences, Inc. Friendswood, TX; [3]Desert Surgical Oncology, Rancho Mirage, CA; [4]Oregon Health & Science University, Portland, OR.

Background: Sentinel lymph node biopsies (SLNB) are performed on patients with cutaneous melanoma to identify early lymphatic metastases. However, current selection criteria based on clinicopathologic features alone leads to many potentially unnecessary surgeries destined to have negative results. With the objective of addressing the clinical need for better SLNB patient selection, we combined clinicopathologic melanoma features with an existing, validated, 31 gene expression test (31-GEP) to create an integrated algorithm (i31-GEP) to better identify the risk of sentinel node melanoma metastasis.

Methods: Using advanced artificial intelligence (R package v3.6.3), a neural network algorithm to predict SLNB positivity was developed (N=1398) and independently validated (N=1674) on T1-T4 tumors by integrating the continuous 31-GEP score with continuous Breslow thickness, mitotic rate, and age and binary ulceration (i31-GEP). Variable importance was determined using the R variable assessment tool for neural networks. Kaplan-Meier analysis and the log-rank test were used to compare patient survival. For accuracy metrics, i31-GEP prediction of <5% was considered a negative result and ≥5% a positive result.

Results: Compared to other covariates assessed within the development cohort, the continuous 31-GEP score had the largest likelihood ratio (G2=91.3, P<.001) followed by Breslow's thickness (G2=53.5, P<.001) and mitotic rate (G2=20.7, P<.001). Within the i31-GEP algorithm, the highest variable importance score was the 31-GEP. Independent validation of the i31-GEP demonstrated alignment of predicted and observed SLN status using linear regression (slope=1.00). Further, the negative predictive value of the i31-GEP was 98.1%, and the yield (positive predictive value) was 14.4%, a 3.4% improvement over the 10.9% pre-test positivity rate. The i31-GEP classified 27.7% of patients as low risk (<5%) compared to only 8.5% of patients identified by T1a disease and no reported high-risk features. For patients initially classified by T-stage as having 5-10% SLN positivity risk, the i31-GEP re-classified 63% of patients as having <5% risk and 10.3% as having >10% positivity risk. In a subset of patients with survival outcomes, patients predicted by the i31-GEP to have <5% risk had significantly higher RFS (97% vs. 88% and 62%, P<.001) than patients predicted to have ≥5% risk and a negative or positive SLN, respectively. Similar results were seen for DMFS (99% vs. 94% and 71%, P=.002), and OS (98% vs. 93% and 82%, P=.043).

Conclusions: The i31-GEP test augments patient classification for risk of melanoma sentinel node metastasis and can be used to improve patient selection for SLNB by integrating the 31-GEP classification test with standard clinicopathologic features.

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20. 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

Sarah T. Arron, MD, PhD[1]; Ashley Wysong, MD[2]; Alison L. Fitzgerald, PhD[3]; Jennifer J. Siegel, PhD[3]; Sarah J. Kurley, PhD[3]; Matthew Goldberg, MD[3]; Sherrif F. Ibrahim, MD, PhD[4]

[1]Sarah Arron, PC, San Mateo, CA; [2]University of Nebraska Medical Center, Omaha, NE; [3]Castle Biosciences, Inc., Friendswood, TX; [4]University of Rochester, Rochester, NY

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 performed 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.

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21. Clinical Utility of a Handheld Elastic Scattering Spectroscopy Tool and Machine Learning on the Diagnosis and Management of Skin Cancer by Primary Care Physicians

Kelly Tepedino, MD[1], Ana Maria Tablada,BS[2], Evan Barnes,[2] Thomaz de Campos Silva FRACGP[4]

[1]Lake City Medical Center:, FL, [2]Dermasensor, Inc.; [3]Kangaroo Point Medical Center, QLD, AU

Background: Skin malignancies are the most common type of cancer diagnosed in the United States and, in recent decades, incidence has been increasing across many parts of the world. [1,2]

Fortunately, it remains highly curable if detected early. Visual inspection with diagnostic aids, such as the ABCDEs of melanoma, remains the standard of care yet accuracy of assessment is dependent upon the clinician's training and experience.[3]

Other methods of skin cancer detection include:

- Non-invasive optical technologies but most are expensive and require extensive training and ongoing skill maintenance.[4]
- Non-invasive specialized form of spectroscopy known as Elastic-Scattering Spectroscopy (ESS) which measures reflected light spectra of a lesion's substructural components.[5]

A portable hand-held ESS device, approved for use in Australia, New Zealand and Europe, uses an algorithm developed through convolutional neural networks CNN (a type of machine learning model) to compare the scan of a lesion under investigation with scans of known benign and malignant lesions.[6,7]

Figure 1. Handheld ESS device

It provides an output of "investigate further" or "monitor'" based upon a lesion's spectral similarities to scans of lesions in the training set.[8]

The algorithm has been trained and validated with 6000 spectral recordings from ~1600 lesions including histologically confirmed melanoma and NMSC; as well as biopsied and unbiopsied benign lesions diagnosed by board-certified dermatologists.[9]

This non-invasive technology has undergone rigorous clinical trials and is easy to use and cost effective for early detection of skin cancer.

Objectives: To test the potential of using a Handheld ESS device which incorporates machine learning to assist in the detection and appropriate management of skin cancer.
To establish whether the use of a Handheld ESS device improves clinicians' detection of skin malignancies by evaluating their clinical performance on cases with suspicious lesions as assessed with and without the output of a Handheld ESS device.

Methods: A total of 57 U.S. board-certified PCP (33 IM (58%), 24 FM (42%) readers with different levels of primary care and dermatology experience participated in this study.

50 cases of skin lesions from different areas of the body were randomly selected from the DERM-ASSESS II Trial.[10]

High resolution digital images of lesions as well as the patient's skin cancer history, risk factors and the results of their physical examinations were presented for each case.

The study was conducted in two phases:

Phase 1: Readers evaluated items listed above for each case without the Handheld ESS device output.

Phase 2: Phase 1 was repeated inclusive of the Handheld ESS device output.

Readers were educated on the Handheld ESS device before evaluating the 50 skin lesion cases in one of five randomly sorted orders during each phase.

After evaluation in each phase, readers completed a questionnaire about their diagnosis (Benign or Malignant), management decision (Lesion's need for further assessment), and confidence level (No confidence, Slight confidence, Moderate confident and High Confidence).

Malignant Lesions	25
Squamous cell carcinoma	9
Basal cell carcinoma	9
Melanoma	4
Severely atypical melanocytic nevus	3

Benign Lesions*	25
Benign melanocytic nevus	3
Benign other	4
Blue nevus	1
Lentigo	2
Seborrheic keratosis	10
Mildly atypical melanocytic nevus	2
Actinic keratosis	3

**13 biopsied and assessed histologically*

**12 diagnosed as benign by dermatologists*

Results: Diagnostic sensitivity of the readers with and without the use of the ESS device was 88% (1261/1425; 95% CI, 84% - 92%) and 67% (958/1425; 95% CI, 62% - 72%), respectively *(Table 1)*.

Table 1. Diagnostic and management performance for detection of skin cancer with and without the use of the Handheld ESS device

	Performance		95% Confidence Interval		P-value
	Without ESS	With ESS	Without ESS	With ESS	
Diagnosis					
Sensitivity %	67 (958/1425)	88 (1261/1425)	62 - 72	84 -92	<.0001
Specificity %	53 (761/1425)	40 (577/1425)	49 - 57	37 - 44	0.0516
Management decision					
Sensitivity %	81 (1160/1425)	94 (1342/1425)	77 - 85	91 - 96	0.0009
Specificity %	36 (516/1425)	31 (437/1425)	31 - 42	28 - 34	0.3558

Note. Data in parentheses are the number of cases correctly identified as malignant (for sensitivity analysis) and benign (for specificity analysis) over the total number of lesions evaluated (25 lesions x 57 readers = 1425)

Management sensitivity of the readers with and without the use of the ESS device was 94% (1342/1425; 95% CI, 91% - 96%) and 81% (1160/1425; 95% CI, 77% - 85%), respectively *(Table 1)*.

Table 2. Shifts in levels of confidence of PCPs in their management decision

Confidence without the device	Confidence Level with the device				
	None	Slight	Moderate	High	Total
None	3	12	20	18	53
Slight	9	91	297	252	649
Moderate	10	138	619	688	1455
High	7	36	118	532	693
Total	29	277	1054	1490	2850

Kappa statistic: 0.1490; OR (95% CI): 4.210 (3.764 to 4.708); p-value: <.0001

Discussion: Maximizing sensitivity in cancer detection is critical given the negative consequences of mismanagement of malignant skin lesions.

Prior publications reviewing non-invasive tools for melanoma detection indicate that spectroscopy achieved best performance in terms of sensitivity (93%, 95% CI 92.8–93.2%) and specificity (85.2%, 95%CI 84.9–85.5%) while reflectance-confocal-microscopy demonstrated good diagnostic performance (sensitivity 88.2%, 80.3–93.1%; specificity 65.2%, 55–74.2%) with better robustness.[11]

Given the high requisite investment in equipment and training for reflectance-confocal-microscopy, it remains out of reach for most PCPs while ease of use and low cost suggest handheld spectroscopy may be a highly acceptable non-invasive tool for the detection of skin malignancies for PCPs.

Use of the ESS device significantly increased the diagnostic sensitivity of readers by 21% ($P < 0.0001$) with no significant difference ($P = 0.0516$) in specificity with and without device use.

Use of the ESS device significantly increased the management sensitivity by 13% ($P = 0.0009$) with no significant difference ($P = 0.3558$) in specificity with and without device use.

Additionally, there is an increase in levels of confidence in management decision with the use of the Handheld ESS device and a direct correlation between this improvement in level of confidence and the correct management of true malignancies.

Conclusion: The study met its primary endpoint of demonstrating that management sensitivity of the PCP with knowledge of the device output is superior to management sensitivity without knowledge of the device output.

The use of the Handheld ESS device in a primary care setting is further supported by a reduction in the subjectivity of the PCPs regarding their evaluations and the limited training required for its use.

Abbreviations: AUC: Area under curve; CNN: Convolutional neural networks ESS: Elastic-scattering spectroscopy; FM: family medicine; IM: internal medicine; PCP: primary care physician; ROC: receiver operating characteristic; SROC: summary receiver operating characteristics

Disclosures: This study was sponsored by DermaSensor Inc.

Author T Silva reports a non-financial advisory relationship with Dermasensor Inc.

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22. Use of Elastic-Scattering Spectroscopy and Machine Learning when Assessing Skin Lesions Suggestive of Skin Cancer

Paul Salmon[1] BHB MBChB FRACP Hon FACD FACMS FNZDSI, Michael Bonning[2] MBBS, FRACGP, BAPPSCI(HONS), MPH, DCH

[1]Skin Center, NZ, [2]Macquarie University, Fellow, AMA NSW, Chair

Introduction and Objectives: Skin malignancies are the most common type of cancer diagnosed in the United States, and Australia and New Zealand lead the world in the number of diagnosed skin malignancies per capita.[1,2] Incidence rates of skin cancer, including malignant melanoma and non-melanoma skin cancer (NMSC), have increased by 44% and 77%, respectively, in recent decades.[3] However, if detected early, skin cancer has proven to be highly curable.

The standard skin cancer diagnosis method is visual inspection with diagnostic aids, but the accuracy is dependent on the clinician's experience.[4] Recently, technology-based methods have been developed that significantly improve the non-invasive diagnosis accuracy, but they require training and/or have high implementation costs.[5] Thus, the challenge is to develop a non-invasive and accurate technology for early skin cancer identification, which is both easy to use and cost-effective.

Elastic-scattering spectroscopy (ESS) is a specialized form of spectroscopy that shows great promise for skin cancer detection,[6] particularly when used with interpretative systems based on machine learning (ML) models, such as convolutional neural networks (CNN). This study evaluates the effectiveness and performance of a hand-held ESS-based device, which uses a spectral classification algorithm, as an objective, non-invasive tool for evaluating patients with skin lesions suggestive of melanoma, basal cell carcinoma, and squamous cell carcinoma.[7]

Materials & Methods: The Handheld ESS device, measures spectra of skin lesions and uses CNN to classify the lesion's scanned properties against those of known malignant and benign lesions. The output of the ESS classifier is "Investigate Further" or "Monitor". Additionally, for "Investigate Further" classified lesions, a score from 1 to 10 is provided which corresponds to the amount of spectral similarity a lesion demonstrates to malignant lesions in studies with 10 representing the highest amount.

The algorithm implemented in the Handheld ESS device was trained and validated using over 11,000 spectral recordings from nearly 2,300 skin lesions, including histologically confirmed melanoma and NMSC; as well as biopsied and unbiopsied benign lesions, as identified or diagnosed by board-certified dermatologists.[6]

Figure 1. Handheld ESS device

A prospective, single-arm, blinded, Investigator-Initiated study was conducted in New Zealand at a single site from 2020-2021 by a board-certified dermatologist. The study included benign lesions deemed to be suggestive of skin cancer to less dermatologically trained clinicians (e.g. primary care physicians) and assessed anatomical, clinical and patient risk factors to diagnose whether a lesion was benign or malignant and recorded how confident the investigator was in his assessment (high vs low).

The Investigator then scanned the lesion with the Handheld ESS device and took a digital photo of the lesion. Lesions considered to be malignant were biopsied per the investigator's standard of care and pathology reports were used to determine final diagnosis.

The clinical endpoints included diagnostic sensitivity and specificity of the Handheld ESS device using dermatologist assessment and pathology results for diagnosis of malignant and benign lesions. Sensitivity is the probability of a malignant lesion being correctly categorized as "Investigate Further". Specificity is the probability of a benign lesion being correctly categorized as "Monitor". Confidence intervals were calculated using the Wilson method, as outlined in Saha et al (2016).[8] to account for potential within-subject correlation. Positive predictive values (PPV) and negative predictive values (NPV) were calculated from these results based upon the trial population.

Further analysis was conducted for "Investigate Further" categorized lesions to examine the PPV across different spectral score range groupings including low (1-5) vs high (6-10), and low (1-3) vs mid (4-7) vs high (7-10). For each spectral score grouping, a frequency value was calculated based upon how often spectral scores for that group appeared.

Results: For this interim analysis, a total of 509 lesions from a private practice serving a heavily sun-damaged population in an area of New Zealand having one of the world's highest incidences of Melanoma[9] were scanned with the Handheld ESS device from February 2020 to July 2021. Final analysis revealed that 89% of the enrolled lesions were benign and 11% were categorized as malignant. There were a variety of lesion types enrolled including Seborrheic keratoses (SK, 43%), Actinic keratoses (AK, 22%), Benign melanocytic nevi (21%), Basal

cell carcinomas (BCC, 7%), Squamous cell carcinomas (SCC, 3%), Melanomas (1.2%) among others. There were no adverse events reported related to device usage. The overall diagnostic sensitivity of the Handheld ESS device in detecting malignant skin lesions was 98.2% (CI: 90.3-100.0%). Overall specificity for detecting benign skin lesions was 46.5% (CI:41.8-51.2%) *(Table 2)*.

Table 1: Concordance Between Device Output and Pathology Results

Device Reading	Pathology Results		Total
	Benign	Malignant	
Benign	211 (46.5%)	1 (1.8%)	212
Malignant	243 (53.5%)	54 (98.2%)	297

The NPV of a Monitor output from the Handheld ESS device was 99.5% (CI: 97.4-99.9%), the associated PPV for all spectral scores in the Investigate Further category was calculated at 18.1% (CI: 14.0-23.1%) and the PPV for the Investigate Further category spectral score range grouping 8-10 was 58.6% (CI: 38.9-76.5%). *(Table 2b, Table 3b)*.

Table 2a: Device Sensitivity and Specificity for Detecting Malignant Lesions

	Result	Exact 95% CI
Specificity	46.5% (211/454)	41.8% to 51.2%
Specificity Excluding AKs	52.6% (181/344)	47.2% to 58.0%
Sensitivity	98.2% (54/55)	90.3% to 100.0%

Table 2b: : Device NPV and PPV with and without AKs for Detecting Malignant Lesions

	Result	Exact 95% CI
NPV	99.5% (211/212)	97.4% to 100.0%
NPV Excluding AKs	99.5% (181/182)	97.0% to 100.0%
PPV	18.2% (54/297)	14.0% to 23.0%
PPV Excluding AKs	24.9% (54/217)	19.3% to 31.2%

Tables below present PPV and frequency distributions for different spectral score groupings *(Table 3 a and b)* of "Investigate Further" categorized lesions in the trial. Across all groupings, a higher spectral score was directly correlated with an increased positive predictive value.

Table 3a Spectral Score Groupings 1-5 and 6-10

Spectral Scores Groupings	PPV	Frequency of 'Investigate Further'
1-5	8.5%	76.8%
6-10	42.4%	23.2%

Table 3b Spectral Score Groupings 1-4, 5-7 and 8-10

Spectral Scores Groupings	PPV	Frequency of 'Investigate Further'
1-4	7.1%	64.2%
5-7	27.9%	28.7%
8-10	58.6%	7.1%

Discussion and Conclusion: The Handheld ESS device's technology has a high sensitivity at 98.2% for detecting malignant skin lesions as demonstrated in this study and a specificity of 46.5%. The negative predictive value of 99% highlights the accuracy of the Handheld ESS device in detecting malignant disease and reassures dermatologists and other clinicians when a "Monitor" output is in concordance with their ongoing clinical evaluation.

The addition of spectral scores to the "Investigate Further" output expands the objective applicability of the Handheld ESS technology and helps inform providers as they conduct their medical decision-making process on appropriate management of a skin lesion found to be suggestive of melanoma, basal cell carcinoma, and/or squamous cell carcinoma.

The study's inclusion of lesions suggestive of skin cancer to those less trained than a dermatologist suggests a potential beneficial role of the device in helping reduce unnecessary biopsies based upon the specificity rate outcomes. Additionally, as a portable, affordable device, the tool's spectral score has the potential to inform prioritization of care for patients with large numbers of pigmented lesions particularly in rural areas where mole mapping may not be available.

The relationship between primary care and specialty care is a critical part of the patient journey particularly for dermatology where accessibility and waiting times pose a general problem.[10] As levels of skin cancer continue to rise in many countries around the world, the use of such a device may contribute to early identification and management of patients presenting with malignant skin lesions and increase efficiency and efficacy of referrals.

Further studies should include a comparison of the device with Dermoscopy on the impact on management accuracy and an evaluation of outcomes when combining Dermoscopy with the device.

Disclosures: This study was supported by a grant from DermaSensor Inc. Authors report financial relationships with the sponsor as investigators and/or advisors.

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23. Tapinarof Cream 1% Once Daily for Plaque Psoriasis: Efficacy by Baseline Disease Characteristics and Demographics in Two Pivotal Phase 3 Trials

Leon Kircik,[1,2] Linda Stein Gold,[3] James Del Rosso,[4] Brad P. Glick,[5] Howard Sofen,[6] Anna M. Tallman,[7] David S. Rubenstein,[7] Philip M. Brown[7]

[1]Skin Sciences PLLC, Louisville, KY, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Henry Ford Health System, Detroit, MI, USA; [4]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV, USA; [5]Herbert Wertheim College of Medicine, Florida International University, Miami, FL, USA; [6]David Geffen UCLA School of Medicine, Los Angeles, CA, USA; [7]Dermavant Sciences, Inc., Morrisville, NC, USA

Introduction: Tapinarof cream 1% once daily (QD) demonstrated highly statistically significant efficacy versus vehicle at 12 weeks and was well tolerated in adults with mild to severe plaque psoriasis in two identical, randomized, double-blind Phase 3 trials: PSOARING 1 (N=510) and PSOARING 2 (N=515). Here, we report results for the primary efficacy endpoint of Physician Global Assessment (PGA) response (0 or 1 and ≥2-grade improvement from baseline) at week 12 by baseline characteristics (PGA score, percentage body surface area [%BSA] affected, duration of disease) and demographics (sex, age, race, and country of enrollment) using pooled data from PSOARING 1 and 2.

Studies: In PSOARING 1 and 2, conducted in the US and Canada, adults with baseline PGA score ≥2 and BSA involvement ≥3–≤20% were randomized 2:1 to tapinarof cream 1% or vehicle QD for 12 weeks. The pooled analysis included the intention-to-treat population assigned to tapinarof 1% QD (n=683) or vehicle (n=342) in PSOARING 1 and 2.

Results: Overall, mean baseline PGA score, %BSA affected, duration of psoriasis and demographics were comparable across treatment groups and studies: most patients (82%) had a PGA score of 3 (moderate), 57% had psoriasis >10 years, and 26% had ≥10% BSA affected; 57% were male, 86% aged <65 years, 85% Caucasian and 76% enrolled in the US. PGA response was 19.94% vs 5.75% (in patients with baseline PGA=2, mild), 40.11% vs 6.35% (baseline PGA=3, moderate), and 36.30% vs 4.69% (baseline PGA=4, severe) in patients treated with tapinarof 1% vs vehicle, respectively. By baseline %BSA affected, PGA response was 38.58% vs 5.12% (baseline BSA <10%) and 35.63% vs 9.25% (baseline BSA ≥10%); and by baseline duration of disease, PGA response was 34.77% vs 7.82% (baseline duration <5 years), 36.92% vs 4.08% (baseline duration 5–10 years), and 39.27% vs 6.48% (baseline duration >10 years) in tapinarof-treated patients vs vehicle, respectively. In addition, PGA response in tapinarof 1% vs vehicle groups was consistent across sex, age, race, and country of enrollment.

Conclusion: Tapinarof cream 1% was consistently efficacious and well tolerated irrespective of baseline PGA score, %BSA affected, duration of psoriasis, sex, age, race, and country of enrolment (US/Canada), supporting its use across a broad spectrum of disease severity and patient populations.

Disclosure: This study was funded by Dermavant Sciences, Inc.

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24. 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

Bruce Strober,[1] Robert Bissonnette,[2] April Armstrong,[3] Linda Stein Gold,[4] Andrew Blauvelt,[5] Leon Kircik,[6,7] Philip M. Brown,[8] Anna M. Tallman,[8] Mark Lebwohl[7]

[1]Yale University, New Haven and Central Connecticut Dermatology Research, Cromwell, USA, [2]Innovaderm Research Inc., Montreal, Canada, [3]Keck School of Medicine at University of Southern California, Los Angeles, USA, [4]Henry Ford Health System, Detroit, USA, [5]Oregon Medical Research Center, Portland, USA, [6]Skin Sciences PLLC, Louisville, USA, [7]Icahn School of Medicine at Mount Sinai, New York, USA, [8]Dermavant Sciences, Inc., Morrisville, USA

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.

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.

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.

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.

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25. Dermatology Provider Shortage and Lack of Melanoma Patient Education in Rural North Carolina

Rachel Tuschak, BS, PA-S

Physician Assistant Student at Drexel University College of Nursing & Health Professions Division of Undergraduate Nursing, Philadelphia, Pennsylvania

Melanoma, the most aggressive type of skin cancer, can metastasize to other areas of the body if undetected and/or untreated.[1] In 2018, in the United States (U.S.), there were 83,996 new cases of melanoma and 8,199 deaths due to melanoma.[2] Additionally, melanoma incidence and mortality rates were greater in rural regions compared to urban regions across the country.[3] Specifically in the state of North Carolina (NC), with 22.7% of its population made up of rural communities, there were 3,032 new cases of melanoma reported in 2018.[2] With these numbers increasing, it is important to note the geographical imbalance of providers, with more working in urban areas, as well as lack of preventative behaviors being practiced by individuals residing in rural regions throughout NC.[4,5]

My project will aim to address the dermatology provider shortage and lack of melanoma education in rural areas in NC. The goals of this project are to advocate for melanoma patient education and to raise awareness of the dermatology provider shortage in rural areas of NC. This project will also aim to enlighten physician assistants (PAs) about the role they can play in rural areas by promoting proper patient education in efforts to improve melanoma outcomes in NC. This information may be applicable on a national level as these interventions could potentially translate to other rural areas across the country. The audience will benefit by becoming more aware of the role they can play in filling this gap in efforts to increase patient education aimed towards rural patient behaviors as well as decrease adverse outcomes related to melanoma.

The first section on the poster will contain data showing the increasing number of melanoma diagnoses in rural areas in NC. The second section will discuss the imbalance of dermatology provider distribution among rural vs. urban areas. It will also show the relationship between dermatology provider density and melanoma mortality rates. The third section will contain information regarding the lack of preventative skin care behaviors in individuals living in rural NC. It will also contain information about the need for patient education addressing modifiable risk factors of melanoma and promoting sun-protective behaviors in rural areas in NC. The final section will explain how PAs can have a role in equalizing the provider imbalance and promoting patient education in efforts to improve melanoma rates in rural NC and other rural areas across the country.

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26. Calcipotriene and Betamethasone Dipropionate Cream Combines High Efficacy, Favorable Safety, and Treatment Preference in a Single Product for Topical Treatment of Psoriasis

Linda Stein Gold[1], Lawrence J. Green[2], Sunil Dhawan[3], Morten Præstegaard[4], Johan Selmer[4]

[1]Dermatology Clinical Research, Henry Ford Health System, Detroit, Michigan, [2]George Washington University School of Medicine, Washington, DC, [3]Center for Dermatology Clinical Research, Fremont, CA and Stanford University School of Medicine, [4]MC2 Therapeutics, Hørsholm, Denmark

Introduction: Calcipotriene and betamethasone dipropionate cream (CAL/BDP; Wynzora® Cream [0.005%/0.064% w/w] is a novel FDA-approved topical treatment for plaque psoriasis based on PAD™ Technology, which has enabled development of a water-containing formulation of CAL and BDP, despite their known pH-related instability when combined in the presence of water. Data from a pivotal phase 3 trial is presented comparing overall efficacy of CAL/BDP cream to CAL/BDP topical suspension (CAL/BDP TS; Taclonex® Topical Suspension).

Methods: CAL/BDP cream was evaluated in a phase 3, randomized, multicenter, investigator-blind trial comparing the efficacy and safety of CAL/BDP cream to vehicle and CAL/BDP TS in adults with psoriasis vulgaris. Patients applied medication once daily for 8 weeks.

The primary efficacy endpoint was the proportion of patients with treatment success at week 8, defined as a minimum 2-point decrease from baseline in Physician Global Assessment (PGA) score to "clear" or "almost clear" disease.

Results: A total of 796 patients were enrolled at 55 clinical sites across the United States. CAL/BDP cream achieved PGA treatment success in 37.4% of patients at week 8, which was significantly greater than CAL/BDP TS (22.8%; p<0.0001) and vehicle (3.7%, p<0.0001). CAL/BDP cream demonstrated significantly greater treatment success at week 4 compared with CAL/BDP TS (24.2% vs 12.9%; p<0.0001). Safety assessments demonstrated that CAL/BDP cream was well tolerated, with an adverse event profile similar to that known for CAL/BDP products.

Conclusions: CAL/BDP cream offers a combination of high efficacy, favorable safety, and excellent treatment convenience in a single product. CAL/BDP cream was significantly more effective than CAL/BDP TS and can be considered a first-line therapy for the topical treatment of psoriasis

Funding: Trial funded by MC2 Therapeutics.

LSG is an investigator, advisor, and/or speaker for MC2 Therapeutics, Leo Pharma, Dermavant, Arcutis, Ortho Dermatologics, Sun Pharma, Amgen, AbbVie, UCB, and BMS. **LJG** is an investigator, speaker, and/or consultant for Amgen, Arcutis, AbbVie, Dermavant, Lilly, MC2 Therapeutics, Novartis, Ortho Dermatologics, Sun Pharma, and UCB. **SD** is an investigator and consultant for AbbVie, Allergan, Galderma, Ortho, BMS, BI, MC2 Therapeutics, Lilly, and Dermira. **MP** and **JS** are employees of MC2 Therapeutics.

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27. Calcipotriene and Betamethasone Dipropionate Cream Demonstrates Clinically Meaningful Improvement of Itch Associated with Psoriasis

Linda Stein Gold[1], Lawrence J. Green[2], Sunil Dhawan[3], Johan Selmer[4], Morten Præstegaard[4]

[1]Dermatology Clinical Research, Henry Ford Health System, Detroit, Michigan, [2]George Washington University School of Medicine, Washington, DC, [3]Center for Dermatology Clinical Research, Fremont, CA and Stanford University School of Medicine, [4]MC2 Therapeutics, Hørsholm, Denmark

Introduction: Calcipotriene and betamethasone dipropionate cream (CAL/BDP; Wynzora® Cream [0.005%/0.064% w/w]) is a novel FDA-approved topical treatment for plaque psoriasis based on PAD™ Technology, which enables a combination of efficacy, safety, and patient preference. Data from a pivotal phase 3 trial is presented for improvement in itch in adults with psoriasis.

Methods: This was a phase 3, randomized, multicenter, investigator-blind trial comparing CAL/BDP cream to vehicle and CAL/BDP topical suspension (TS) (Taclonex® Topical Suspension) in adult patients with psoriasis vulgaris. Patients applied study medication once daily for 8 weeks. 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 a ≥4-point improvement in peak pruritus NRS score from baseline.

Results: The trial enrolled 796 patients, which included 626 patients with a peak pruritus NRS score ≥4 at baseline. CAL/BDP cream demonstrated superior reduction of peak pruritus NRS score compared with vehicle at week 4 (3.5- vs 1.1-point improvement; p<0.0001), as well as at weeks 1 and 8 (both p<0.0001). A higher proportion of patients achieved a clinically relevant improvement of ≥4 points from baseline to week 4 in the CAL/BDP cream group versus vehicle (60.3% vs 21.4%; p<0.0001). CAL/BDP cream further demonstrated a significantly greater proportion of patients achieving a ≥4-point 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).

Conclusions: CAL/BDP cream, a novel topical treatment for 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.

Funding: Trial funded by MC2 Therapeutics.

LSG is an investigator, advisor, and/or speaker for MC2 Therapeutics, Leo Pharma, Dermavant, Arcutis, Ortho Dermatologics, Sun Pharma, Amgen, AbbVie, UCB, and BMS. **LJG** is an investigator, speaker, and/or consultant for Amgen, Arcutis, AbbVie, Dermavant, Lilly, MC2 Therapeutics, Novartis, Ortho Dermatologics, Sun Pharma, and UCB. **SD** is an investigator and consultant for AbbVie, Allergan, Galderma, Ortho, BMS, BI, MC2 Therapeutics, Lilly, and Dermira. **MP** and **JS** are employees of MC2 Therapeutics.

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

Lawrence F. Eichenfield, MD,[1,2] Eric L. Simpson, MD, MCR,[3] Kim Papp, MD, PhD,[4] Jacek C. Szepietowski, MD, PhD, FRCP (Edin),[5] Leon Kircik, MD,[6] Darryl Toth, MD,[7] Seth B. Forman, MD,[8] Michael E. Kuligowski, MD, PhD, MBA,[9] May E. Venturanza, MD,[9] Haobo Ren, PhD,[9] Amy S. Paller, MD[10]

[1]Departments of Dermatology and Pediatrics, University of California San Diego; [2]Rady Children's Hospital; [3]Oregon Health & Science University; [4]K. Papp Clinical Research and Probity Medical Research; [5]Department of Dermatology, Venereology, and Allergology, Wroclaw Medical University; [6]Icahn School of Medicine at Mount Sinai; [7]XLR8 Medical Research and Probity Medical Research; [8]ForCare Clinical Research; [9]Incyte Corporation; [10]Northwestern University Feinberg School of Medicine

Introduction: Atopic dermatitis (AD), a highly pruritic inflammatory skin disease, often begins in childhood and persists into adolescence and adulthood. Ruxolitinib cream is a topical selective 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] 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 (as-needed treatment; 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 only skin with active AD and stopped treatment 3 days after clearance of lesions. Patients restarted AD treatment at first recurrence. Here, long-term disease control and safety of 0.75%/1.5% ruxolitinib cream in adolescents (aged 12–17 years) who continued their original ruxolitinib cream regimen during the LTS period in TRuE-AD1 (assessed for disease control, n=46/n=41) and TRuE-AD2 (n=43/n=36) were evaluated. Most patients in the 0.75%/1.5% ruxolitinib cream groups had no/minimal skin lesions (IGA 0/1 [clear/almost clear skin]) during Weeks 8–52 in TRuE-AD1 (range, 59.0%–78.8%/57.1%–78.4%) and TRuE-AD2 (range, 51.2%–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 over 52 weeks, with a consistent safety profile throughout the study period. As-needed monotherapy with ruxolitinib cream provided adequate long-term disease control in adolescents with AD.

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29. Long-Term Safety and Disease Control with Ruxolitinib Cream in Atopic Dermatitis: Results from Two Phase 3 Studies

Kim Papp, MD, PhD,[1] Jacek C. Szepietowski, MD, PhD, FRCP (Edin),[2] Leon Kircik, MD,[3] Darryl Toth, MD,[4] Lawrence F. Eichenfield, MD,[5] Seth B. Forman, MD,[6] Michael E. Kuligowski, MD, PhD, MBA,[7] May E. Venturanza, MD,[7] Kang Sun, PhD,[7] Eric L. Simpson, MD, MCR[8]

[1]K. Papp Clinical Research and Probity Medical Research; [2]Department of Dermatology, Venereology and Allergology, Wroclaw Medical University; [3]Icahn School of Medicine at Mount Sinai; [4]XLR8 Medical Research and Probity Medical Research; [5]Departments of Dermatology and Pediatrics, University of California San Diego; [6]ForCare Clinical Research; [7]Incyte Corporation; [8]Oregon Health & Science University

Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease. Ruxolitinib cream is a topical selective 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 in the 0.75%/1.5% ruxolitinib cream groups had no or minimal skin lesions (IGA 0/1 [clear/almost clear skin]) 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 in the 0.75% (n=426) and 1.5% (n=446) ruxolitinib cream groups, 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 had no or minimal skin lesions, 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 monotherapy. Ruxolitinib cream was well tolerated in the long-term setting.

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30. Assessing Long-term Maintenance of Efficacy with Tralokinumab Monotherapy in Patients with Moderate-to-severe Atopic Dermatitis: Combined Results from Two Phase 3, Randomized, Double-blind, Placebo-controlled Trials (ECZTRA 1 and 2)

Andrew Blauvelt,[1] Andreas Wollenberg,[2] Andrew Pink,[3] Ketty Peris,[4] April Armstrong,[5] Lynda Spelman,[6] Hidehisa Saeki,[7] Charles Lynde,[8] Pedro Herranz,[9] Sebastien Barbarot,[10] Eric Simpson[11]

[1]Oregon Medical Research Center, Portland, OR, USA; [2]Ludwig-Maximilian University of Munich, Munich, Germany; [3]St. John's Institute of Dermatology, Guy's and St. Thomas' Hospitals, London, UK; [4]Catholic University and Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy; [5]Keck School of Medicine at the University of Southern California,

Los Angeles, CA, USA; [6]Veracity Clinical Research, Brisbane, Queensland, Australia, and Probity Medical Research, Woolloongabba, Queensland, Australia; [7]Nippon Medical School, Tokyo, Japan; [8]Lynde Dermatology, Probity Medical Research, Markham, Ontario, Canada, and University of Toronto, Ontario, Canada; [9]Hospital Universitario La Paz, Madrid, Spain; [10]Centre Hospitalier Universitaire de Nantes, Nantes, France; [11]Oregon Health & Science University, Portland, OR, USA

Introduction: In two pivotal trials, ECZTRA 1 (NCT03131648) and 2 (NCT03160885), tralokinumab monotherapy was superior to placebo for all primary and secondary endpoints at week 16 in adults with moderate-to-severe AD (Wollenberg A, et al. Br J Dermatol. 2021;184:437-449). The objectives of this analysis were to evaluate the maintenance of efficacy beyond 16 weeks of tralokinumab monotherapy in patients with AD who were initial responders, and to assess whether reduced dosing frequency of tralokinumab from q2w to q4w has an impact on maintenance of efficacy.

Methods: High-responding patients achieving Investigator's Global Assessment (IGA) 0/1 or Eczema Area and Severity Index (EASI)-75 at week 16 on tralokinumab q2w were rerandomized in the maintenance phase 2:2:1 to tralokinumab q2w, q4w, or placebo for 36 weeks. A prespecified, pooled analysis assessed maintenance of response (IGA 0/1 or EASI-75) at week 52. Rescue medication use, including topical corticosteroids (TCS), was considered non-response. Post hoc analysis of time to relapse was conducted.

Results: A large proportion of high-responding patients (n=337) continuing tralokinumab q2w or q4w maintained response without any rescue medication (including TCS) at week 52. With q2w, 56.2% maintained IGA 0/1 or EASI-75 (difference = 26.3% vs placebo; P<0.001) at week 52. With q4w, 50.0% maintained IGA 0/1 or EASI-75 (difference = 20.7% vs placebo; P=0.003). Time to relapse based on IGA 0/1 and EASI-75 was prolonged with tralokinumab vs placebo (q2w, P=0.004 and q4w, P=0.14; q2w, P=0.002 and q4w, P=0.044, respectively). Overall, adverse event frequency was similar for tralokinumab q2w (73%), q4w (66%), and placebo (70%).

Conclusion: Initial response to tralokinumab was maintained at high levels at week 52 without TCS use and was well tolerated. Step-down to q4w dosing may be an option for some patients.

Funding: The ECZTRA 1 and 2 studies were sponsored by LEO Pharma A/S, Ballerup, Denmark.

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31. COVID-19 in Tralokinumab-treated Patients with Moderate-to-severe Atopic Dermatitis: Case Series from the ECZTEND Long-term Extension Trial

Andrew Blauvelt,[1] Andrew Pink,[2] Margitta Worm,[3] Richard Langley,[4] Antonio Costanzo,[5] Le Gjerum,[6] Emilie Jorgensen,[6] Joshua Corriveau,[7] Emma Guttman-Yassky[8]

[1]Oregon Medical Research Center, Portland, OR, USA; [2]St. John's Institute of Dermatology, Guy's and St. Thomas' Hospitals, London, UK; [3]Charité–Universitätsmedizin Berlin, Berlin, Germany; [4]Dalhousie University, Halifax, NS, Canada; [5]Humanitas University, Milan, Italy and Humanitas Research Hospital IRCCS, Milan, Italy; [6]LEO Pharma A/S, Ballerup, Denmark; [7]LEO Pharma, Madison, NJ, USA; [8]Icahn School of Medicine at Mount Sinai, New York, NY, USA

Introduction: There is special interest in the impact of coronavirus disease 2019 (COVID-19) on individuals with chronic, immune-mediated diseases such as atopic dermatitis (AD). There have been concerns that patients treated with immunomodulatory therapies for these diseases may have increased risk of developing COVID-19 or more severe disease with worse outcomes following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The objective of this case series is to describe the outcomes of patients diagnosed with COVID-19 while participating in the tralokinumab long-term extension trial, ECZTEND (NCT03587805).

Methods: Approximately 1600 patients with moderate-to-severe AD are participating in the ongoing, multinational, open-label ECZTEND study. We report a case series of 51 adult patients with moderate-to-severe AD who had confirmed cases of COVID-19 during treatment with tralokinumab q2w. Patients were not required to discontinue tralokinumab following a COVID-19 diagnosis if continuation was deemed appropriate by the investigator. This is an interim analysis of data collected through February 26, 2021.

Results: A total of 22 male and 29 female patients were diagnosed with COVID-19 through February 2021. Mean age was 37.7 years (range, 19-70 years); mean body-mass index was 27.6 (range, 16.3-50.8). Regarding comorbid diseases, 30 patients (59%) had asthma and 5 (10%) had hypertension. Cardiovascular (CV) disease was present in 2 patients, and chronic obstructive pulmonary disease (COPD) and diabetes were present in 1 patient each. COVID-19 severity was predominantly mild (68.6%) or moderate (27.5%), and all patients with mild or moderate disease recovered fully. The two patients (3.9%) who experienced severe cases had multiple risk factors and comorbidities, including obesity, COPD, and CV disease. Both were hospitalized and subsequently recovered (one with sequelae); neither case was reported as related to tralokinumab treatment. Mean duration of COVID-19 infection was 15 days (range, 1-39 days). All 51 patients (100%) continued tralokinumab treatment, the majority (75%) without dose interruption following COVID-19 diagnosis.

Conclusions: COVID-19 cases were predominately mild or moderate (96%), and all patients continued tralokinumab treatment following COVID-19 diagnosis.

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

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32. Long-term Improvements Observed in Tralokinumab-treated Patients with Moderate-to-severe Atopic Dermatitis: An ECZTEND Interim Analysis

Andrew Blauvelt,[1] Jean-Philippe Lacour,[2] Darryl Toth,[3] Vivian Laquer,[4] Stefan Beissert,[5] Andreas Wollenberg,[6] Pedro Herranz,[7] Andrew Pink,[8] Ketty Peris,[9] Stine Fangel,[10] Hidehisa Saeki[11]

[1]Oregon Medical Research Center, Portland, OR, USA; [2]University Hospital of Nice Côte d'Azur, Nice, France; [3]Probity Medical Research, Windsor, Ontario, Canada; [4]First OC Dermatology, Fountain Valley, CA, USA; [5]University of Dresden, Dresden, Germany; [6]Ludwig-Maximilian University of Munich, Munich, Germany; [7]Hospital Universitario La Paz, Madrid, Spain; [8]St John's Institute of Dermatology, Guy's and St. Thomas' Hospitals, London, UK; [9]Institute of Dermatology, Catholic University of the Sacred Heart, Rome, Italy; [10]LEO Pharma A/S, Ballerup, Denmark, [11]Nippon Medical School, Tokyo, Japan

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. The efficacy and safety of tralokinumab for up to 52 weeks in adult patients with AD have been published previously.[1,2] 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 long-term efficacy and safety results based on Investigator's Global Assessment (IGA) and Eczema Area and Severity Index (EASI) scores.

Methods: Outcomes were analyzed as observed at Week 56 and included all patients enrolled 60 weeks prior to data cut-off (N=612).

Results: Overall, 1174 patients were included in ECZTEND at data cut-off (April 2020). Median time since last treatment dose in parent trials[1-3] 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 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 ongoing ECZTEND study is sponsored by LEO Pharma A/S, Ballerup, Denmark.

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1. Wollenberg A, et al. Br *J Dermatol*. 2021;184:437-449.
2. Silverberg JI, et al. Br *J Dermatol*. 2021;184:450-463.
3. Merola JF, et al. *J Am Acad Dermatol*. 2021;85:71-78

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33. Long-term Proactive Treatment of Plaque Psoriasis Vulgaris with Calcipotriene/Betamethasone Dipropionate Foam was Associated with Prolonged Time in Remission and Reduced Number of Relapses

Richard B. Warren MD, Ph.D,[1] Kim A. Papp MD, FRCPC, Ph.D,[2] Marie H. Mørch MS[3]

[1]The Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, University of Manchester, Manchester, United Kingdom , [2]Probity Medical Research and K Papp Clinical Research, Waterloo, Ontario, Canada, [3]LEO Pharma A/S, Ballerup, Denmark

Introduction: The Phase III PSO-LONG study (NCT02899962) demonstrated superior efficacy of proactive management (PM) of psoriasis with twice-weekly calcipotriene 0.005%/betamethasone dipropionate 0.064% (Cal/BD) foam vs reactive management (RM) with twice-weekly vehicle foam; patients from both treatment groups received 4-weeks of once-daily Cal/BD foam for relapse.[1] We projected the clinical course of patients from PSO-LONG over a 1-year period using a multistate model.

Methods: Data were analyzed using a multistate model (msm package in R).[2] The model considers four states: remission (physician's global assessment [PGA]<2), relapse (PGA≥2), end-of treatment (completion/withdrawal), and treatment failure (PGA≥2 following relapse treatment), with covariates of treatment group, PGA at randomization and pooled sites. Assessments included estimated mean and total duration of time in remission or relapse and expected number of relapses in the PM vs RM groups.

Results: Estimated mean (SE) time in remission was 81.3 (6.7) and 48.9 (3.9) days for PM and RM, respectively; time in relapse was similar for both groups (30.4 [2.8] vs 30.0 [2.6] days, respectively). The total estimated number of days in remission was 36 greater for PM vs RM: 224.1 and 188.0 respectively; with total estimated number of days in relapse 34 fewer for PM vs RM: 62.2 and 96.2 respectively. The expected number of relapses was 2.0 (mean exposure: 248.8 days) with PM versus 3.2 (mean exposure: 238.7 days) for RM.

Conclusion: PM with Cal/BD foam provided superior efficacy vs RM in prolonging time in remission and reducing number of relapses and total time spent in relapse.

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Commercial Disclosure Information: Funded by LEO Pharma A/S, Ballerup, Denmark.

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34. Long-term Treatment of Plaque Psoriasis with Calcipotriene/Betamethasone Dipropionate Foam was Locally Well Tolerated and Not Associated with Skin Atrophy

Leon Kircik MD,[1] Marie Holst Mørch MS,[2] Bibi Petersen MD Ph.D,[2] Monika Liljedahl MD Ph.D,[2] Andreas Wollenberg MD[3]

[1]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA, [2]LEO Pharma Ballerup A/S, Ballerup, Denmark, [3]Department of Dermatology and Allergology, Ludwig Maximilian University Munich, Munich, Germany

Introduction: Skin atrophy is a concern when prescribing potent topical corticosteroids long term. In this post hoc analysis of the PSO-LONG study (a double-blind,

vehicle-controlled study evaluating safety and long-term management of psoriasis with calcipotriene 0.005%/ betamethasone dipropionate 0.064% [Cal/BD foam]; NCT02899962),[1] we evaluated skin atrophy and local tolerability.

Methods: PSO-LONG included a 4-week, open-label phase of once-daily (QD) Cal/BD foam, followed by a 52-week maintenance phase with patients randomized to twice-weekly Cal/BD foam QD (proactive management) or vehicle foam QD (reactive management), with 4 weeks Cal/BD foam QD for relapse.[1] Physician assessments of skin atrophy and local skin reactions (dryness, erosion, erythema and edema), and patient assessments of burning/pain, were conducted at regular visits (every 4 weeks) or at relapse.

Results: When evaluating regular visits (non–relapse-related), for patients receiving Cal/BD (n=272) vs vehicle foam (n=273), physicians reported no dryness (97.0% vs 95.6%), no erosion (98.9% vs 99.0%), no erythema (96.2% vs 96.1%) and no edema (98.7% vs 98.6%); furthermore, patients reported no burning/pain (96.6% vs 92.8%, respectively). At the start and end of relapses, local skin reactions and burning/pain were present at slightly higher levels than non-relapse-related visits, but were still absent for the majority of patients in both treatment groups, with cases usually mild. No investigator-reported skin atrophy was reported at any point, in either treatment group.

Conclusion: Cal/BD foam, was well tolerated when used as either reactive or proactive management for up to 52 weeks, with a low incidence of local skin reactions and burning/pain, and no reports of skin atrophy.

Reference:

1. Lebwohl M, et al. *J Am Acad Dermatol*. 2021;84:1269-1277.

Commercial Disclosure Information: Funded by LEO Pharma A/S, Ballerup, Denmark.

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35. Evaluating Complete Control of Urticaria with Ligelizumab: A Composite Score of Symptoms and Quality-of-life Outcome

Giménez-Arnau A.M.[1], Maurer M.[2], Bernstein J.[3], Sitz K.[4], Hide M.[5], Sussman G.[6], Acharya S.[7], Terradas-Montana P.[8], Severin T.[9]

[1]Hospital del Mar, IMIM, Universitat Autònoma Barcelona, Barcelona, Spain, [2]Dermatogical Allergology, Allergie-Centrum-Charité, Charité – Universitätsmedizin, Berlin, Germany, [3]University of Cincinnati College of Medicine and Bernstein Clinical Research Center, Cincinnati, OH, United States , [4]Rock Allergy and Asthma Clinic, Little Rock, Arkansas, United States , [5]Hiroshima University, Hiroshima, Japan, [6]University of Toronto, Toronto, Ontario, Canada , [7]Novartis Healthcare Pvt. Ltd., Hyderabad, India, [8]Novartis Farmaceutica, S.A., Barcelona, Spain, [9]Novartis Pharma AG, Basel, Switzerland

Background: Assessing the holistic effect of treatment in patients with chronic spontaneous urticaria (CSU) requires evaluating different patient-reported outcomes (PROs), including effect on symptoms and quality of life. Weekly PROs such as the Hive Severity Score (HSS7), Itch Severity Score (ISS7), Angioedema Activity Score (AAS7), and Dermatological Life Quality Index (DLQI) are used to evaluate patients with CSU. These PROs correlate, but patients may not always exhibit the same magnitude of response for each instrument. We assessed complete urticaria control using a composite of these PROs.

Methods: The ligelizumab (LIG) Phase 2b trial was a dose-finding, multicenter, randomized, double-blind, active, and placebo (PBO)-controlled study. Adult patients with moderate-to-severe CSU disease activity (UAS7≥16), uncontrolled with H1 antihistamines, were randomized to subcutaneous LIG 24mg, 72mg, or 240mg, omalizumab (OMA) 300mg, or PBO every 4 weeks (wks) for 20 wks, or single-dose LIG 120mg. Combining established and validated scores into a composite outcome was used to evaluate complete control and response to treatment (no multiplicity adjustments and nominal p values). A patient free from signs and symptoms of urticaria with concurrent HSS7=0, ISS7=0, and AAS7=0 was considered to have CSU completely controlled. Concurrent DLQI=0–1 indicated being CSU-free.

Results: At wk 12, the proportion of patients showing CSU completely controlled was 44.1% with LIG 72mg (p=0.007 vs. OMA, and 0.003 vs. PBO), 40.0% with LIG 240mg (p=0.025 vs. OMA, and 0.004 vs. PBO), 23.5% with OMA (p=0.021 vs. PBO) and 0.0% with PBO. The proportion of CSU-free patients was 38.1% with LIG 72mg (p=0.008 vs. OMA, and 0.006 vs. PBO), 35.3% with LIG 240mg (p=0.020 vs. OMA, and 0.007 vs PBO), 18.8% with OMA (p=0.035 vs. PBO) and 0.0% with PBO. At wk 20, the proportion of patients with CSU completely controlled was 33.3%, 34.1%, 25.9%, and 4.7%, and for CSU-free patients was 32.1%, 31.8%, 23.5%, and 4.7% for LIG 72mg, 240mg, OMA, and PBO, respectively. During the treatment free follow-up, at wk 28, the proportion of patients remaining CSU-free for LIG 72mg, 240mg, OMA, and PBO was 22.8%, 25.0%, 5.3%, and 4.9%, respectively.

Conclusion: LIG was more likely to achieve and sustain complete control on all PROs vs. OMA or PBO. Using a composite score of validated PROs for CSU can be useful in clinical studies for differentiating response to treatments.

Acknowledgments: Medical writing support was provided by Ooi Poh Sien (Novartis Corp Sdn Bhd, Kuala Lumpur) and Mohammad Fahad Haroon (Novartis Healthcare Ltd., Hyderabad) and was funded by Novartis Pharmaceuticals Corporation. This abstract was developed in accordance with Good Publication Practice (GPP3) guidelines. Authors had full control of the content and made the final decision on all aspects of this publication.

Funding Source: This investigation was sponsored by Novartis Pharma AG, Basel, Switzerland. The editorial and medical writing support was funded by Novartis Pharma AG, Switzerland, in accordance with GPP3 guidelines.

Author Financial Disclosures: **AMG** reports roles as a Medical Advisor for Uriach Pharma, Sanofi and Genentech, Novartis, FAES, GlaxoSmithKline, Amgen, Thermo Fisher and has research grants supported by Uriach Pharma, Novartis, and Instituto Carlos III- FEDER; she also participates in educational activities for Uriach Pharma, Novartis, Genentech, Menarini, Leo Pharma,

GlaxoSmithKline, MSD, Almirall, Avene and Sanofi.
MM is or recently was a speaker and/or advisor for and/or has received research funding from Amgen, Allakos, Aralez, AstraZeneca, Celldex, FAES, Genentech, GIInnovation, Kyowa Hakko Kirin, Leo Pharma, Menarini, Novartis, Moxie, MSD, Roche, Sanofi, Third Harmonic, UCB, and Uriach.
JB reports grants and personal fees from Novartis, AstraZeneca, Allakos, Amgen, Celldex, Genentech, and Sanofi Regeneron outside the submitted work.
KS has received research grants from AstraZeneca, BioCryst, GlaxoSmithKline, Novartis and provided consultancy to BioCryst Pharmaceuticals Inc.
MH has received lecture and/or consultation fees from Taiho Pharmaceutical, Novartis, MSD, Teikoku Seiyaku, Mitsubishi Tanabe Pharma, Uriach, and Kyowa Hakko Kirin.
GS has received research support from Aimmune, Amgen, AstraZeneca, DBV technologies, Genentech, Kedrion S.p.A, Leo Pharma, Novartis, Nuvo Pharmaceuticals Inc., Sanofi, Stallergenes, Merck, Schering-Plough, Regeneron, and ALK; is a medical advisor and/or has received payment for lectures from Merck, Novartis, CSL Behring, Pfizer, Anaphylaxis Canada, the Allergy Asthma and Immunology Society of Ontario and the Canadian Hereditary Angioedema Network.
SA is an employee of Novartis Healthcare Pvt. Ltd., Hyderabad, India.
PTM is an employee of Novartis Farmaceutica, S.A., Barcelona, Spain.
TS is an employee of Novartis Pharma AG, Basel, Switzerland.

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36. Psoriatic Arthritis: The Role of the Non-Physician Clinician in the Diagnosis and Treatment of Patients With Psoriasis

Michael D. Overcash, MPAS, PA-C,[1] Christopher Chillura, MSPAS, PA-C,[1] Sarah P. Fender, MSPAS, PA-C,[1] Matthew K. Ewald, MSPAS, PA-C,[1] Aiken McDowell McNair, MSPAS, PA-C,[1] Michelle Nye, MSPAS, PA-C,[1] Clint Blankenship, PharmD, PA-C, RPh, DFAAPA[1]

[1]College of Health Professions, Medical University of South Carolina, Charleston, SC

Background: Psoriatic arthritis is a clinically heterogeneous, chronic, and progressive disease that develops in up to 30% of patients with psoriasis and is characterized by multiple and increasing joint defects caused by persistent immune-mediated inflammation. Several treatment options are available, including multiple biologic agents that inhibit specific cellular mediators of inflammation either directly or indirectly. Early detection and intervention are critical to preventing severe joint damage and pain, necessitating increased awareness and education about this disease for primary providers and nonphysician clinicians. Physician assistants and nurse practitioners, given their role in the primary care setting and within multiple specialty areas such as dermatology and rheumatology, are often the first to see patients who may have psoriatic arthritis. These healthcare providers are increasingly important in the early diagnosis and treatment of this disease.

Methods: In this review, we provide an overview of psoriasis and psoriatic arthritis and discuss the multiple treatment options that are available for these patients.[1] We also discuss ways to help recognize early joint involvement in the clinic and emphasize the role that nonphysician clinicians play in the care of patients with psoriatic arthritis.

Results: Psoriasis is a complex disease that extends beyond skin manifestations. A substantial proportion of patients with psoriasis develop PsA and are at risk of experiencing irreversible and disabling joint damage. Therefore, early diagnosis and intervention with therapies that effectively treat all aspects of psoriatic disease are necessary in these patients. Physician assistants and nurse practitioners in dermatology and rheumatology—who are well positioned to recognize psoriatic arthritis early, treat patients, and prevent long-term complications—benefit from education on recognizing and treating psoriatic disease to improve outcomes. Biologics have demonstrated efficacy in several disease domains of psoriatic arthritis, and treatment guidelines generally recommend their use over that of nonbiologic agents.

Conclusions: Nonphysician clinicians are well positioned to identify patients with PsA and increasingly play larger roles in the early diagnosis, treatment, and education of these patients. Further utilization of nonphysician clinicians is needed to improve the care of patients with psoriatic disease.

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37. Long-term Management of Plaque Psoriasis: Maintenance of Treatment Success After Cessation of Fixed-Combination Halobetasol Propionate and Tazarotene Lotion

Douglas DiRuggiero,[1] Jayme Heim,[2] Linda Stein Gold,[3] Mark G. Lebwohl,[4] Neal Bhatia,[5] Abby Jacobson,[6] Radhakrishnan Pillai[7]

[1]Skin Cancer and Cosmetic Dermatology Center, Rome, GA; [2]West Michigan Dermatology, Grandville, MI; [3]Henry Ford Hospital, Detroit, MI; [4]Icahn School of Medicine at Mount Sinai, New York, NY; [5]Therapeutics Clinical Research, San Diego, CA; [6]Ortho Dermatologics (a division of Bausch Health US, LLC), Bridgewater, NJ; [7]Bausch Health US, LLC, Petaluma, CA

Introduction: Psoriasis is a chronic relapsing-remitting disease that can have a substantial effect on quality of life due to both physical symptoms and psychological burden. As such, there is a need for therapies that provide a rapid onset of response, long-term therapeutic effect, and continued safety and efficacy should longer durations of treatment or retreatment be needed. Fixed-combination halobetasol propionate (0.01%) and tazarotene (0.045%) lotion (HP/TAZ) is approved for treatment of plaque psoriasis in adults. Because this topical combination may mitigate adverse effects of chronic steroid use and tazarotene-related irritation, it is promising as a long-term treatment. Here, we examined the maintenance of treatment effect after HP/TAZ treatment cessation.

Methods: In a 52-week open-label study (NCT02462083), participants with plaque psoriasis were treated with once-daily HP/TAZ for 8 weeks. Participants with treatment success (defined as investigator's global assessment [IGA] score of clear [0] or almost clear [1]) discontinued treatment for 4 weeks. At week 12, all participants were reevaluated for ≥1-grade improvement in IGA from baseline; those without improvement were discontinued from the study, whereas those with improvement continued the study and were managed in 4-week cycles (ie, those who did not achieve treatment success continued receiving once-daily HP/TAZ, whereas those who achieved treatment success did not receive treatment until the next evaluation). Maximum continuous exposure was 24 weeks. In this post hoc analysis, maintenance of treatment success was evaluated after HP/TAZ cessation in participants who were enrolled ≥8 weeks and achieved an IGA of clear at ≥1 visit.

Results: Of 550 participants, 318 (57.8%) achieved treatment success at some point during the study; 54.4% of participants achieved treatment success by week 8. Fifty-six participants were enrolled ≥8 weeks and achieved an IGA of clear at ≥1 visit. Among these participants, after achieving the first IGA of clear, 28.6% did not require any HP/TAZ retreatment; 53.6%, 62.5%, and 83.9% did not require retreatment for ≥85, ≥57, and ≥29 days, respectively. After retreatment, 9 of 37 participants who relapsed (24.3%) achieved an IGA of clear (mean time to reachieve clear, 11.6 weeks). The most common treatment-related adverse events among the 56 participants who achieved an IGA of clear at ≥1 visit were application site reactions. At week 52, most participants had no burning (89.3%), itching (66.1%), or dryness (69.6%).

Conclusions: Over 52 weeks, 53.6% of participants who achieved clear skin with HP/TAZ did not require retreatment for >12 weeks. HP/TAZ was well tolerated and most participants were symptom free at the end of the study period.

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38. Retreatment with Brodalumab Results in Skin Clearance and Improvements in Quality of Life in Patients with Psoriasis after Treatment Interruption

April Armstrong,[1] Brian Keegan,[2] George Han,[3] Abby Jacobson[4]

[1]University of Southern California, Los Angeles, CA; [2]Princeton Dermatology Associates, Monroe, NJ; [3]Department of Dermatology at Mount Sinai Beth Israel, New York, NY; [4]Ortho Dermatologics (a division of Bausch Health US, LLC), Bridgewater, NJ

Introduction: Psoriasis is a chronic inflammatory skin disease that negatively impacts quality of life, leading to significant physical burden. Brodalumab is a fully human anti–interleukin-17 receptor A monoclonal antibody efficacious for the treatment of moderate-to-severe plaque psoriasis. Treatment interruption is a common real-life experience in individuals with psoriasis. This analysis presents efficacy and health-related quality of life data after brodalumab withdrawal and retreatment.

Methods: In a double-blind, placebo-controlled study (NCT01708590; AMAGINE-1), patients with moderate-to-severe psoriasis were randomized to brodalumab 210 mg or placebo every 2 weeks (Q2W). At week 12, patients receiving brodalumab who achieved a static physician's global assessment (sPGA) of 0 or 1 were rerandomized to their induction dose of brodalumab or placebo. Beginning at week 16, all rerandomized patients who experienced return of disease (sPGA ≥3) qualified for retreatment and received an induction dose of brodalumab. Efficacy was assessed by psoriasis area and severity index (PASI) and quality of life was evaluated with the dermatology life quality index (DLQI).

Results: A total of 79 patients randomized to brodalumab 210 mg Q2W in the induction phase and rerandomized to placebo in the withdrawal phase experienced return of disease. Of the patients who exhibited PASI 75% improvement from baseline (PASI 75) before withdrawal of brodalumab (n=38), 92.1% (95% CI, 78.6% to 98.3%) achieved PASI 75, 86.8% (95% CI, 71.9% to 95.6%) achieved PASI 90, and 65.8% (95% CI, 48.6% to 80.4%) achieved PASI 100 16 weeks after reinitiation of brodalumab 210 mg Q2W. Among those who reached PASI 100 with initial treatment (n=21), 90.5% (95% CI, 69.6% to 98.8%) achieved PASI 100 16 weeks after reinitiation of brodalumab 210 mg Q2W. Mean (SE) baseline DLQI scores in patients in the retreatment population who experienced previous biologic failure (n=18) or nonfailure (n=61) before entering the study, respectively, were 14.1 (1.9) and 12.9 (0.8), which improved to 1.9 (1.1) and 1.8 (0.4) at week 52 (similar to DLQI scores achieved during the induction phase at week 12). Change from baseline DLQI scores were -11.5 (95% CI, -15.6 to -7.4) and -11.0 (95% CI, -12.8 to -9.2) for the 2 groups, respectively.

Conclusion: Most patients with psoriasis who experienced a return of disease after brodalumab withdrawal returned to their previous levels of response 16 weeks after reinitiation of brodalumab. Improvement in quality of life was maintained after retreatment, regardless of exposure to previous biologic treatment.

Funding: This study was sponsored by Ortho Dermatologics. Medical writing support was provided by MedThink SciCom and funded by Ortho Dermatologics. Ortho Dermatologics is a division of Bausch Health US, LLC.

Previous presentation information: Data included in this abstract have been previously presented in part at the 44th Annual Hawaii Dermatology Seminar®; February 16-21, 2020; Maui, HI.

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39. Tazarotene 0.045% Lotion for Acne: Formulation, Application Characteristics, and Clinical Efficacy and Safety

Zoe D. Draelos, MD[1]; Emil A. Tanghetti, MD[2]; Linda Stein Gold, MD[3]; Hilary Baldwin, MD[4,5]; Leon H. Kircik, MD[6,7,8]; Eric Guenin, PharmD, PhD, MPH[9]

[1]Dermatology Consulting Services, PLLC, High Point, NC; [2]Center for Dermatology and Laser Surgery, Sacramento, CA; [3]Henry Ford Hospital, Detroit, MI; [4]The Acne Treatment

and Research Center, Brooklyn, NY; [5]Robert Wood Johnson University Hospital, New Brunswick, NJ; [6]Indiana University School of Medicine, Indianapolis, IN; [7]Physicians Skin Care, PLLC, Louisville, KY; [8]Icahn School of Medicine at Mount Sinai, New York, NY; [9]Ortho Dermatologics, Bridgewater, NJ*

**Ortho Dermatologics is a division of Bausch Health US, LLC*

Background: Tazarotene (TAZ) 0.045% lotion is the most recently approved retinoid for the treatment of acne. It was developed using polymeric emulsion technology to provide uniform and rapid distribution of TAZ and moisturizing/hydrating excipients across the skin. Tolerability of this formulation may be improved by vehicle design and the lower dose of TAZ used compared with all other TAZ formulations.

Objectives: Review the formulation, efficacy, safety, application characteristics, and subject perception of TAZ 0.045% lotion across multiple studies.

Methods: The vehicle lotion for TAZ 0.045% was assessed for skin hydration and epidermal barrier maintenance (via in vivo corneometry and transepidermal water loss; N=30); subject perception was evaluated via questionnaire (N=15). Skin coverage with TAZ 0.045% lotion was compared to trifarotene 0.005% cream in a double-blind split-body study (N=30). In vivo skin deposition of TAZ was assessed 6 hr post-application of TAZ 0.045% lotion and TAZ 0.1% cream (N=10); tape strips were used to serially remove skin layers across epidermis and analyzed for TAZ. In a 12-week phase 2 clinical trial, participants (≥12 years; N=210) were randomized to TAZ 0.045% lotion, TAZ 0.1% cream, lotion vehicle, or cream vehicle. Lesion count reductions, treatment success, and adverse events (AEs) were assessed.

Results: The vehicle for TAZ 0.045% significantly improved skin moisture content and barrier function vs untreated skin as early as 15 min post-application. Subjects also perceived the vehicle as moisturizing, hydrating, non-greasy, and lightweight. Tazarotene 0.045% lotion was highly spreadable, covering on average almost 30% more skin than the same amount of trifarotene cream. After application of both 0.045% lotion and 0.1% cream, TAZ concentration was highest at the skin surface, though concentration was ~2-fold higher for cream than lotion at all skin layers. These findings are consistent with clinical trial data, in which TAZ 0.045% lotion had comparable efficacy but approximately half the rate of treatment-related AEs as 0.1% cream.

Conclusions: TAZ 0.045% lotion utilizes polymeric emulsion technology to enhance hydration, moisturization, and skin barrier function. There is superior tolerability of TAZ 0.045% lotion versus TAZ 0.1% cream, with similar clinical efficacy. This easy-to-apply lotion appears to have enhanced skin coverage compared with trifarotene cream. Overall, this TAZ lotion formulation is an effective and well tolerated option for the treatment of acne, with sensory and aesthetic properties preferred by patients.

Funding: Ortho Dermatologics.

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40. Therapeutic Recommendations for the Treatment of Toenail Onychomycosis in the US

Shari R. Lipner, MD, PhD[1]; Warren S. Joseph, DPM[2]; Tracey C. Vlahovic, DPM[3]; Richard K. Scher, MD1; Phoebe Rich, MD[4]; Mahmoud Ghannoum, PhD[5]; C. Ralph Daniel, MD[6]; Boni Elewski, MD[7]

[1]Department of Dermatology, Weill Cornell Medicine, New York, NY; [2]Arizona College of Podiatric Medicine, Midwestern University, Glendale, AZ; [3]Temple University School of Podiatric Medicine, Philadelphia, PA; [4]Oregon Health and Science University, Portland, OR; [5]Case Western Reserve University, and University Hospitals Cleveland Medical Center, Cleveland, OH; [6]Department of Dermatology, University of Mississippi Medical Center, Jackson, MS; [7]University of Alabama at Birmingham School of Medicine, Birmingham, AL

Introduction: Onychomycosis—a fungal infection of the nail bed or plate—affects up to 14% of individuals in North America. It is undertreated and treatment is challenging as toenail growth can take up to 12 months or more, the nail plate may prevent drug penetration, and disease recurrence is common. National guidelines and consensus documents on onychomycosis diagnosis and treatment were last published more than 5 years ago in 2014 (British) and 2015 (Canadian)—around the time that both topical efinaconazole and tavaborole were first approved in the US in 2014. Since then, more clinical data, post hoc analyses, meta-analyses, and FDA-approved indications have become available for onychomycosis drugs. As such, updated medical guidance is needed.

Methods: This document aims to provide recommendations for the diagnosis and pharmaceutical treatment of toenail onychomycosis following a roundtable discussion (on March 15, 2021) with a panel of dermatologists, podiatrists, and a microbiologist specializing in nail disease.

Results: There was a general consensus on several topics regarding onychomycosis diagnosis, confirmatory laboratory testing, and medications. Onychomycosis should be assessed clinically and confirmed with microscopy, histology, and/or culture. Efinaconazole 10% is the primary choice for topical treatment and terbinafine the primary choice for oral treatment. Efinaconazole can also be considered for off-label use for maintenance to prevent recurrences. For optimal outcomes, patients should be counseled regarding treatment expectations as well as follow-up care and maintenance post-treatment.

Conclusions: These therapeutic recommendations—based on new clinical data— provide important updates to previous guidelines/consensus documents to assist healthcare practitioners in the diagnosis and treatment of toenail onychomycosis.

Funding: Ortho Dermatologics

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41. Applied Scholarly Project Proposal

Parth S. Patel, DMSc, MPAS, PA-C

Abstract: The purpose of this paper to introduce the topic of my applied scholarly project. The applied scholarly project will be focus on a case presentation from the clinic. This case study is regarding a 53-year-old African

American female with a PMHx of DM Type 2, who presents to the dermatology clinic complaining of erythematous, oval plaques with slight scaling noted to her shoulders bilaterally. Additionally, she presents with erythematous and violaceous subcutaneous tender nodules to the scalp x 2 months. Cutaneous lesions of sarcoidosis can present similarly to other conditions such as eczema or psoriasis, and there are numerous variations to cutaneous presentation. The information will be applied to efficiently diagnose and determining the best possible treatment for cutaneous sarcoidosis in conjunction with dermatology, rheumatology, pulmonology and family medicine specialties.

Introduction: The purpose of this applied scholarly project will be to determine the best possible appropriate treatment plan options for a patient diagnosed with cutaneous sarcoidosis in conjunction with rheumatology, dermatology and pulmonology. Patients will require comprehensive treatment and monitoring.

Topic: Sarcoidosis is a multisystem, granulomatous, inflammatory condition which can affect various organ systems.[6] There are numerous clinical manifestations of cutaneous sarcoidosis, with the most common form being popular sarcoidosis presenting as red-brown, violaceous papules on the face, trunk or extremities. Nodular sarcoidosis is another common clinical manifestation which presents with erythematous or flesh colored subcutaneous nodules consisting of collection of granulomas, generally on the upper extremities. The lower extremities typically present with lesions called erythema nodosum which are tender and erythematous nodules. Less common clinical manifestations include maculopapular sarcoidosis, plaque sarcoidosis, atrophic or ulcerative sarcoidosis, verrucous sarcoidosis, and perforating sarcoidosis.[1,2,6] There have been reported cases of sarcoidosis arising at special locations such as: scars, tattoos, nails and alopecia.[1,2,6]

It is important that an accurate diagnosis is made when patients present with cutaneous lesions due to the way in which sarcoidosis affects multiple organ systems. A patient diagnosed with sarcoidosis will typically require comprehensive care with dermatology, rheumatology and pulmonology, and other specialties as needed. The clinical presentation can help determine a list of working differential diagnosis such as psoriasis, lichen planus, nummular eczema, granuloma annulare, cutaneous T-cell lymphoma. Therefore, it is essential to make the accurate diagnosis through appropriate biopsies and blood work.[1-5,6]

Audience : The audience of this applied scholarly project will be physician assistants, nurse practitioners, and physicians who practice dermatology, rheumatology, pulmonology and primary care practitioners. As all three specialties would be involved in the treatment and management of sarcoidosis.

Purpose: The purpose of this applied scholarly project will be to explore the various treatment options available for patients diagnosed with either cutaneous or systemic sarcoidosis. This will be conducted via literature review to determine the best possible clinical therapeutic options for these patients.

Significance for the Profession: Comprehensive treatment for patients diagnosed with sarcoidosis is very important to ensure there is no sequalae. Treatment options for sarcoidosis can be variable and will vary from patient to patient due to co-morbidities and severity. Many of the treatment options are considered to be immunosuppressive agents such as methotrexate, oral prednisone, and hydroxychloroquine. Therefore it is essential for patients to receive close follow up with necessary specialists and have blood work done as deemed appropriate.

Main Ideas: The main idea this project will convey to its audience will be the recent treatment and management guidelines for sarcoidosis. Sarcoidosis is a multisystem, granulomatous, inflammatory condition which can affect various organ systems.[6] Given the ability of sarcoidosis to affect various organ systems it is crucial that the patient is started on the appropriate topical and oral therapies. Various treatment options include: Intralesional Kenalog (ILK), topical calcineurin inhibitors, and topical corticosteroid therapy. Oral options include: antimalarial drugs, methotrexate, oral tetracyclines and oral corticosteroids. For refractory cases, there are some studies that support the use of TNF-alpha inhibitors such as infliximab.[5]

Scope: The scope of this project will be applicable to areas of family medicine, dermatology, pulmonology, rheumatology and ophthalmology. Cutaneous lesions of sarcoidosis can present similarly to other conditions such as eczema or psoriasis and therefore there can be a delay in initial diagnosis. Therefore is important that this diagnosis is made early on in its course.

Potential Submission: Potential journal publications for this applied scholarly project will be: *JAAPA (Journal of the American Academy of PAs), JDPA (Journal of Dermatology for Physician Assistants)*. I will also consider journals for rheumatology, pulmonology and ophthalmology.

Conclusion: The goal of this applied scholarly project will be to explore the current guidelines in treatment and management of sarcoidosis comprehensively with pulmonology, dermatology, rheumatology and family medicine specialties to ensure the best clinical outcome for the patient. Overall it is important for patients with sarcoidosis to follow up with various subspecialties to prevent further sequalae.

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42. Dupilumab and Live-Attenuated Vaccines: Experience With Prior Dupilumab Use and Yellow Fever Vaccine in Patients With Severe Asthma From Brazil

Michael E. Wechsler[1], Lisa Purcell[2], Adelmir Souza-Machado[3], Christine Xu[4], Xuezhou Mao[4], Upender Kapoor[4], Faisal A. Khokhar[2], John T. O'Malley[5], Veronica Mas Casullo[2], Leda P. Mannent[6], Elizabeth Laws[4], Megan Hardin[5]

[1]National Jewish Health, Denver, CO, USA; [2]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [3]Universidade Federal da Bahia, Salvador, Brazil; [4]Sanofi, Bridgewater, NJ, USA; [5]Sanofi, Cambridge, MA, USA; [6]Sanofi, Chilly-Mazarin, France

Background: Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4/IL-13, key and central drivers of type 2 inflammation in multiple diseases. The single-arm, open-label extension study LIBERTY ASTHMA TRAVERSE (NCT02134028) evaluated long-term safety, tolerability, and efficacy of dupilumab in adult and adolescent patients with moderate-to-severe asthma who had previously completed a dupilumab asthma study. The safety and tolerability of concomitant use of live-attenuated vaccines with dupilumab have not been previously evaluated. Due to a yellow fever outbreak in Brazil during TRAVERSE, enrolled patients requiring yellow fever vaccine (YFV) discontinued dupilumab to receive YFV and continued to be monitored for safety and efficacy endpoints. This post hoc analysis describes the experience of these patients, including the neutralizing antibody response and the safety profile and tolerability of the live-attenuated YFV in these patients.

Methods: Patients at risk discontinued dupilumab and were vaccinated with a single injection of the 17D live-attenuated YFV. Dupilumab serum concentrations, plaque reduction neutralization titers (PRNT), and safety signals before and after YFV were evaluated.

Results: 37 patients (mean [SD] age 46.5 years [12.0]; 32.4% male) discontinued dupilumab treatment to receive YFV. Dupilumab concentrations were assessed in most patients 1–25 days before (n = 16) and on the same day of (n = 19) vaccination. Pre- and post-YFV PRNT were obtained in 23/37 and 37/37 patients, respectively. Time from last dose of dupilumab to YFV administration was 7–51 days (mean [SD] 22.3 [11.9]). Of the 23 patients with pre- and post-YFV PRNT, 15 had dupilumab concentrations obtained on the day of YFV administration; mean dupilumab concentration (76.4 mg/L) exceeded the therapeutic threshold (37.4 mg/L). All patients were seropositive after receiving YFV, with the response appearing unaffected by pre-YFV dupilumab concentrations. No YFV-related adverse events were reported in 36/37 (97.3%) patients; 1 patient reported non-serious body ache, malaise, and dizziness 7 days after YFV and fully recovered. There were no reports of vaccine hypersensitivity.

Conclusions: These data suggest that dupilumab had no apparent impact on the immunologic response to the live-attenuated YFV. Further studies are warranted to investigate the effect of dupilumab on live-vaccine-induced immune responses.

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43. Dupilumab Improves Family Quality of Life in Children Aged 6–11 Years With Severe Atopic Dermatitis (LIBERTY AD PEDS)

Lawrence F. Eichenfield[1,2], Eric L. Simpson[3], Charles W. Lynde[4,5], Zhen Chen[6], Noah A. Levit[6], Chien-Chia Chuang[7], Carden Simcox[6], Randy Prescilla[7], Zhixiao Wang[6]

[1]University of California, San Diego, CA, USA; [2]Rady Children's Hospital, San Diego, CA, USA; [3]Oregon Health and Science University, Portland, OR, USA; [4]University of Toronto, Markham, ON, Canada; [5]Lynderm Research, Markham, ON, Canada; [6]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [7]Sanofi Genzyme, Cambridge, MA, USA

Objective: To assess the effect of treatment with dupilumab on the quality of life (QoL) of the pediatric patient's caregiver(s)/family.

Methods: In LIBERTY AD PEDS (NCT03345914), 367 patients with severe AD aged ≥6 to <12 years received subcutaneous dupilumab every 2 weeks (q2w; 100mg if baseline weight <30kg, 200mg if ≥30kg); every 4 weeks (q4w, 300mg); or placebo; for 16 weeks. Patients received concomitant medium-potency topical corticosteroids (TCS). Only data for FDA-approved dose regimens are shown. The Dermatitis Family Impact (DFI) questionnaire is a disease-specific measure assessing the impact of AD on QoL of the caregiver(s)/family of AD-affected children.

Results: At baseline, mean total DFI scores reported by caregiver(s)/family in patients weighing <30kg for dupilumab 300mg q4w+TCS/placebo+TCS groups were 17.7/16.1. In patients weighing ≥30kg, the scores for dupilumab 200mg q2w+TCS/placebo+TCS groups were 13.5/14.0. Baseline DFI scores showed a significant impact of AD on QoL of the patient's caregiver(s)/family. At Week 16, DFI scores were significantly improved in patients receiving dupilumab+TCS vs patients receiving placebo+TCS. In patients <30kg, least squares (LS) mean percent change (SE) in DFI scores for dupilumab 300mg q4w+TCS/placebo+TCS groups were –73.4(5.6)/–38.7(6.8) (P <0.0001 vs placebo). In patients ≥30kg, LS mean percent change (SE) in DFI scores for dupilumab 200mg q2w+TCS/placebo+TCS groups were –75.4(5.0)/–40.6(5.9) (P <0.0001 vs placebo). The safety profile was consistent with the known dupilumab safety profile in adults and adolescents.

Conclusion: Dupilumab treatment in children aged ≥6 to <12 years with severe AD resulted in significant improvement in QoL of the patient's caregiver(s) and family.

44. Dupilumab Induces Clinically Meaningful Improvement in Symptoms of Anxiety and Depression in Children With Severe Atopic Dermatitis

Lawrence F. Eichenfield[1,2], Michael J. Cork[3], Melinda Gooderham[4,5], Andreas Wollenberg[6], Zhen Chen[7], Noah A. Levit[7], Chien-Chia Chuang[8], Randy Prescilla[8], Zhixiao Wang[7]

[1]University of California, San Diego, CA, USA; [2]Rady Children's Hospital, San Diego, CA, USA; [3]University of Sheffield, Sheffield, UK; [4]SKiN Centre for Dermatology, Peterborough, ON, Canada; [5]Queen's University, Kingston, ON, Canada; [6]University Hospital, LMU Munich, Munich, Germany; [7]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [8]Sanofi Genzyme, Cambridge, MA, USA.

Background: Atopic dermatitis (AD) is associated with anxiety and depression in patients of all ages, including children. In children with severe AD, treatment of AD may improve mental health. We report the effect of treatment with dupilumab in combination with medium-potency topical corticosteroids (TCS) in children aged ≥6 to <12 years with severe AD and moderate-to-severe anxiety or depression.

Methods: In the phase 3 LIBERTY AD PEDS trial (NCT03345914), 367 patients with severe AD aged ≥6–<12 years received subcutaneous dupilumab every 2 weeks (q2w; 100 mg if baseline weight <30kg, 200 mg if ≥30kg); every 4 weeks (q4w, 300 mg); or placebo; with concomitant TCS for 16 weeks. Only data for FDA-approved dose regimens are shown, vs weight-matched placebo. Proxy-reported symptoms, behaviors, and feelings of mental health were assessed using Patient-Reported Outcome Measurement Information System (PROMIS) Pediatric Anxiety and Depression instruments. The severity of anxiety and depression was categorized into the following groups based on PROMIS Pediatric Anxiety and Depression scores: ≤50 normal; >50–≤55 mild; >55–≤65 moderate; >65 severe. The minimal clinically important difference was defined as ≥9-point and ≥8-point change from baseline in PROMIS Pediatric Anxiety and PROMIS Pediatric Depression, respectively. This analysis includes patients with moderate-to-severe PROMIS Pediatric Anxiety or Depression scores at baseline.

Results: At baseline, a large proportion of patients in all treatment groups reported moderate-to-severe levels of anxiety and/or depression (<30kg placebo: 67.2%; <30kg q4w: 67.2%; ≥30kg placebo: 62.9%; ≥30kg q2w: 61.0%). Within this subgroup of patients with moderate-to-severe anxiety or depression at baseline, the proportions achieving clinically meaningful improvement in both PROMIS Pediatric Anxiety and Depression scores vs placebo after 16 weeks of treatment were: <30kg q4w vs placebo, 68.3% vs 36.6% ($P < 0.01$); ≥30kg q2w vs placebo, 55.6% vs 35.9% ($P = 0.085$). Within the same subgroup, proportions of patients achieving normal scores in the PROMIS Pediatric Anxiety and Depression measures at Week 16 were: <30kg q4w/placebo, 48.8%/31.7%; ≥30kg q2w/placebo, 44.4%/30.8%. The safety profile in this study was acceptable and consistent with the known dupilumab safety profile.

Conclusion: In this population of children aged ≥6–<12 years with severe AD, approximately 60–70% experienced moderate-to-severe anxiety and/or depression scores at baseline. A substantially greater proportion of patients with moderate-to-severe anxiety or depression at baseline treated with dupilumab+TCS for 16 weeks achieved clinically meaningful improvements in both PROMIS Pediatric Anxiety and Depression scores vs placebo+TCS.

45. Analysis of Efficacy Outcomes Using ERIVANCE-like Methodology in Patients with Locally Advanced Basal Cell Carcinoma

Reinhard Dummer,[1] Aaron S Farberg,[2] Ralf Gutzmer,[3] James Spencer,[4] Felix Kiecker,[5] Alexander Guminski,[6,7] Kurt Gebauer,[8,9] Carmen Loquai,[10] Caroline Robert,[11] Dirk Schadendorf,[12] Nicholas Squittieri,[13] Ramon Arntz,[14] Serena Martelli,[14] Michael Migden[15]

[1]Skin Cancer Center University Hospital, Zürich, Switzerland; [2]Baylor University Medical Center, TX; [3]Johannes Wesling Clinic Minden, Minden, Germany; [4]Spencer Dermatology and Skin Cancer Center, FL; [5]Charité Universitätsmedizin, Edmund-Lesser-Haus, Berlin, Germany; [6]Royal North Shore Hospital, St Leonards, Australia; [7]The University of Sydney, Sydney, Australia; [8]University of Western Australia, Perth, Australia; [9]Probity Medical Research, Waterloo, Canada; [10]University Medical Center Mainz, Mainz, Germany; [11]Institut Gustave Roussy and Paris-Saclay University, Villejuif, France; [12]University Hospital, Essen, Germany; [13]Sun Pharmaceutical Industries, Inc., NJ; [14]Sun Pharmaceutical Industries, BV, Hoofddorp, Netherlands; [15]University of Texas MD Anderson Cancer Center, TX

Background: Sonidegib is a hedgehog pathway inhibitor (HHI) approved in the US, EU, Switzerland, and Australia for adult patients with locally advanced basal cell carcinoma (laBCC) not amenable to curative surgery or radiotherapy. The BOLT study for sonidegib used mRECIST for laBCC tumor evaluation. In contrast, the ERIVANCE trial for vismodegib, another HHI, used a combination endpoint of a reduction of ≥30% in externally visible tumor or radiographic dimension (RECIST criteria), or complete resolution of ulceration. The algorithm used to determine overall response varies between the two, and mRECIST utilizes more stringent methods of tumor assessment, resulting in efficacy outcomes with lower responses vs RECIST. We present a preplanned sensitivity analysis from BOLT applying ERIVANCE-like criteria to tumor outcomes in patients with laBCC receiving sonidegib 200 mg once daily (QD).

Methods: The primary endpoint was objective response rate (ORR), while secondary assessments included best overall response (complete response [CR], partial response [PR], stable disease [SD], and progressive disease [PD]). laBCC tumors were evaluated using mRECIST criteria utilizing MRI, color photography, and histological assessment and re-analyzed with ERIVANCE-like criteria. Per mRECIST, CR was based on negative histology on multiple punch biopsies, CR, PR, or SD (scar/fibrosis only) per photographic assessment, and an MRI response of

either CR or not available (NA). Per the ERIVANCE-like criteria, CR was based on negative histology and CR, PR, SD, or NA for MRI assessment and photographic evaluation. In contrast, any MRI outcome other than CR or NA in addition to negative histology and CR, PR, or SD (scar/fibrosis only) was considered PR per mRECIST, whereas it was CR using ERIVANCE-like criteria.

Results: Per mRECIST criteria, ORR (95% confidence interval [CI]) for patients receiving sonidegib 200 mg (n=66) was 56.1% (43.3%–68.3%). Three patients achieved CR; PR, SD, and PD were reached in 34, 23, and 1 patient, respectively. In comparison, efficacy outcomes using RECIST criteria were overall higher with an ORR (95% CI) of 60.6% (47.8%–72.4%). Similarly, 14 patients reached CR. PR, SD, and PD occurred in 26, 20, and 1 patient, respectively.

Conclusions: Overall, applying ERIVANCE-like criteria to patients with laBCC receiving sonidegib 200 mg QD resulted in higher response rates compared with using mRECIST criteria.

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46. Cardiovascular Events, Serious Infections, and Neoplasia through 5 Years of Tildrakizumab Exposure in Two Phase 3 Clinical Trials

Eingun James Song,[1] Cynthia Trickett,[2] Kurt Gebauer,[3] Ronald B Vender,[4] Robert Gniadecki,[5] Jennifer Cather,[6] Dario Kivelevitch,[7] Darren T West,[8] Stephen J Rozzo,[9] and Sunil Dhawan[10]

[1]North Sound Dermatology, Mill Creek, WA, USA; [2]University of Texas Southwestern Medical Center, Dallas, TX, USA, and University of North Texas Health Science Center, Fort Worth, TX, USA; [3]Fremantle Dermatology, Fremantle, Western Australia, Australia, and Probity Medical Research, Waterloo, ON, Canada; [4]Department of Medicine, Division of Dermatology, McMaster University, Hamilton, ON, Canada, and Dermatrials Research Inc., Hamilton, ON, Canada; [5]Division of Dermatology, University of Alberta, Edmonton, AB, Canada; [6]Modern Research Associates, Dallas, TX, USA; [7]Baylor Scott & White Health, Dallas, TX, USA; [8]Spectrum Dermatology, Scottsdale, AZ, USA; [9]Sun Pharmaceuticals, Inc., Princeton, NJ, USA; [10]Center for Dermatology Cosmetic & Laser Surgery, Milpitas, CA, USA, Department of Dermatology, Stanford University, Stanford, CA, USA, and Center for Dermatology Clinical Research, Inc., Fremont, CA, *USA*

Background: Tildrakizumab (TIL) is an anti–interleukin-23p19 monoclonal antibody approved for treatment of plaque psoriasis.[1–3]

Objective: To assess incidence of cardiovascular events, infections, and neoplasia in patients receiving TIL for up to 5 years in reSURFACE 1 and reSURFACE 2 (NCT01722331/NCT01729754).

Methods: reSURFACE 1/2 were 3-part, randomized, double-blind, placebo-controlled, phase 3 trials with optional long-term extensions evaluating TIL 100 (TIL100) or 200 mg (TIL200) monotherapy at week (W)0, W4, and every 12W thereafter in adults with moderate to severe chronic plaque psoriasis.[1] This post hoc analysis reports exposure-adjusted incidence rates (EAIR) of positively adjudicated cardiovascular events, infections, and neoplasia as cumulative incidence per 100 patient-years (100PY) of exposure to TIL100 or TIL200 in patients receiving ≥1 dose of tildrakizumab during the extensions.

Results: In the reSURFACE 1/2 extensions, 239/381 patients received TIL100 with total exposure of 1164.8/1671.3 PY and 267/349 patients received TIL200 with total exposure of 1365.8/1567.5 PY. In patients receiving TIL100 in reSURFACE 1/2, the EAIRs were 0.5/0.3 per 100PY for both major adverse cardiovascular events (MACE) and extended MACE (including unstable angina, coronary revascularization, and resuscitated cardiac arrest). For reSURFACE 1/2 patients receiving TIL200, EAIRs were 0.4/0.6 per 100PY for MACE and 0.7/0.6 per 100PY for extended MACE. The EAIRs of serious adverse event (SAE) infections were 0.8/0.9 per 100PY for patients receiving TIL100 and 1.0/1.0 per 100PY for patients receiving TIL200 in reSURFACE 1/2; EAIRs for serious neoplasia in reSURFACE 1/2 were 1.6/0.8 per 100PY following TIL100 and 0.8/1.1 per 100PY following TIL200.

Conclusions: Through 5 years of reSURFACE 1 and reSURFACE 2, EAIRs of MACE, SAE infections, and neoplasia were low and similar between TIL doses.

Sponsorship: The studies were funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; analyses were funded by Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA.

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47. Hematology Laboratory Shift Based on Common Terminology Criteria in Patients with Advanced Basal Cell Carcinoma Receiving Sonidegib 200 mg Daily: Results from the 42-month BOLT Study

Michael Migden[1], Karl Lewis[2], Alexander Guminski[3,4,5], Ralf Gutzmer[6], Carmen Loquai[7], Nicholas Squittieri[8], Peter Foley[9, 10, 11]

[1]University of Texas MD Anderson Cancer Center, Departments of Dermatology, Division of Internal Medicine, and Head and Neck Surgery, Division of Surgery, Houston, TX, USA; [2]University of Colorado Cancer Center, Anschutz Medical Campus, Aurora, CO, USA; [3]Department of Oncology, Royal North Shore Hospital, St Leonards, Australia; [4]Melanoma Institute Australia, The University of Sydney, Sydney, Australia; [5]Mater Hospital, Sydney, Australia; [6]Skin Cancer Center Hannover, Department of Dermatology, Hannover Medical School, Hannover, Germany; [7]Department of Dermatology, University Medical Center Mainz, Mainz, Germany; [8]Medical Affairs Oncology and Long Term Care, Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA; [9]Department of Dermatology, St Vincent's Hospital Melbourne, Fitzroy, Victoria, Australia; [10]The University of Melbourne, Parkville, Victoria, Australia; [11]Skin Health Institute Inc, Carlton, Victoria, Australia

Background: Sonidegib, a Hedgehog pathway inhibitor, is approved to treat patients with locally advanced basal cell carcinoma (BCC) not amenable to curative surgery or radiotherapy. Here we present hematology laboratory

shifts in patients with advanced BCC receiving sonidegib 200 mg once daily (QD).

Methods: BOLT was a randomized, double-blind, multicenter, phase 2 study with patients randomized 1:2 to receive sonidegib 200 or 800 mg orally QD, respectively. Hematology assessments were performed bi-weekly for 14 weeks, then every 4 weeks until week 77, then followed as clinically indicated until end of treatment. Hematology evaluations were performed by a central laboratory. Safety assessments included adverse event monitoring.

Results: Through 42 months of treatment with sonidegib 200 mg (n=70), 24.1% and 7.6% of patients had grade 1 or 2 anemia vs 3.8% and 0% of patients had grade 1 or 2 hyperhemoglobinemia. Zero patients had a grade 3 or 4 hemoglobin shift. Overall, 16.5%, 8.9%, and 2.5% of patients had grade 1, 2, or 3 lymphocytopenia; 0% had grade 4 shift. Grade 1 or 2 neutropenia was detected in 6.3% and 1.3% of patients, respectively; 0% had grade 3 or 4. Overall, 6.3% and 1.3% of patients had grade 1 or 4 thrombocytopenia, respectively, while 0 patients had grade 2/3. Grade 1 or 2 leukopenia was observed in 5.1% and 1.3% of patients, respectively; 0% had grade 3/4 shifts.

Conclusions: Through 42 months of treatment with sonidegib 200 mg QD, most patients experienced no hematology changes or grade 1 hematology shifts.

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48. Bimekizumab Efficacy and Safety Up to Two Years in Patients with Moderate to Severe Plaque Psoriasis Switching from Ustekinumab: Results from the Interim BE BRIGHT Open-label Extension Trial

Craig Leonardi,[1] Paul G. Sator,[2] Akimichi Morita,[3] Georgios Kokolakis,[4] Andrew Blauvelt,[5] Richard B. Warren,[6] Dirk De Cuyper,[7] Cynthia Madden,[8] Veerle Vanvoorden,[7] Maggie Wang,[8] Kim A. Papp[9]

[1]Central Dermatology and Saint Louis University School of Medicine, MO, USA; [2]Clinic Hietzing, Vienna, Austria; [3]Nagoya City University Graduate School of Medical Sciences, Japan; [4]Charite-Universitatsmedizin, Berlin, Germany; [5]Oregon Medical Research Center, OR, USA; [6]Salford Royal NHS Foundation Trust, The University of Manchester, UK; [7]UCB Pharma, Belgium; [8]UCB Pharma, NC, USA; [9]Probity Medical Research and K Papp Clinical Research, ON, Canada

Introduction: We report efficacy and safety data up to two years for patients from the BE VIVID phase 3 trial who switched from ustekinumab (UST) to bimekizumab (BKZ), without washout, upon entering the BE BRIGHT open-label extension (OLE).

Methods: Patients were randomized to UST 45mg/90mg at Weeks (Wks) 0/4, then Q12W, or BKZ 320mg Q4W through Wk52 in BE VIVID, and subsequently entered the OLE. In the OLE, patients were re-randomized to BKZ 320mg Q4W or Q8W based on Wk52 PASI90 response.

Wk52–100 (OLE Wk0–48) data are reported. We report PASI100 responses for patients who switched from UST to BKZ (UST/BKZ switchers) or received BKZ continuously (BKZ/BKZ) in the OLE. PASI90 and PASI100 responses are presented for UST/BKZ switchers who were PASI90 non-responders at the end of BE VIVID (Wk52). Data are presented by initial BE VIVID randomization group (BKZ or UST) regardless of BKZ OLE maintenance dosing regimen. Data are reported using non-responder imputation. Safety data are reported.

Results: Of the 141 UST-randomized and 283 BKZ-randomized patients who completed the maintenance perioid of BE VIVID, 136 and 276 entered the OLE, respectively. Upon entering the OLE at Wk52, 44.9% UST and 73.6% BKZ patients achieved PASI100.

Among UST/BKZ switchers, PASI100 response increased (65.4% at Wk56) after switching to BKZ, comparable to BKZ/BKZ patients at Wk68 through Wk100 (UST/BKZ switchers: 78.7% and 69.9%, respectively; BKZ/BKZ: 75.4% and 68.8%).

Among the 44 UST/BKZ Wk52 PASI90 non-responders, PASI90 and PASI100 responses were rapidly achieved at Wk56 after the first BKZ dose (PASI90: 77.3%; PASI100: 40.9%). Response was sustained and further improved to Wk100 (PASI90: 84.1%; PASI100: 54.5%).

Through Wks52–100, incidences of serious treatment emergent adverse events (TEAEs) were 7.4% in UST/BKZ switchers and 7.2% with BKZ/BKZ. One BKZ/BKZ death occurred which was not considered treatment-related. The most common TEAEs in the OLE were nasopharyngitis (UST/BKZ: 22.8%; BKZ/BKZ: 21.7%), oral candidiasis (13.2%; 15.6%), and upper respiratory tract infection (8.8%; 6.5%). Oral candidiasis cases were mild/moderate; none led to discontinuation.

Conclusion: After switching to BKZ in the OLE, response rates in UST/BKZ switchers were improved and, after 16 wks, were comparable to BKZ/BKZ patients. UST/BKZ Wk52 PASI90 non-responders showed substantial, rapid, and sustained improvements upon switching to BKZ. There were no unexpected safety findings in UST/BKZ switchers during the first year of the OLE.

Funding: UCB Pharma.

Disclosures:

CL: Speaker (honoraria) for AbbVie, Celgene, Eli Lilly and Novartis; served as an investigator for Actavis, AbbVie, Amgen, Boehringer Ingelheim, Celgene, Coherus, Corrona, Dermira, Eli Lilly, Galderma, Glenmark, Janssen, LEO Pharma, Merck (MSD), Novartis, Novella, Pfizer, Sandoz, Stiefel and Wyeth; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Dermira, Eli Lilly, Janssen, LEO Pharma, Pfizer, Sandoz, UCB Pharma and Vitae.

PGS: Has been an advisor and/or received speaker honoraria or travel expense reimbursements and/or received grants and/or participated in clinical trials for AbbVie, Actelion, ALK, Almirall, Amgen, Celgene, Eli Lilly, Galderma, Gilead, Janssen, LEO Pharma, Merck (MSD), Maruho, Novartis and UCB.

AM: Received research grants, consulting fees, and/or speaker's fees from AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eisai, Eli Lilly, Janssen, Kyowa Hakko Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Nichi-Iko, Nippon Kayaku, Novartis, Pfizer, Sun Pharma, Taiho Pharmaceutical, Torii Pharmaceutical, Ushio and UCB Pharma.

GK: Received travel grants or honoraria or has been a

consultant member of advisory boards and speaker's bureaus or has served as investigator for AbbVie, Actelion, Basilea, Biogen, Boehringer Ingelheim, Celgene, Eli Lilly, Hexal-Sandoz, Janssen, LEO Pharma, Merck (MSD), Novartis, Pfizer and UCB Pharma.

AB: Served as a scientific adviser and/or clinical study investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Evommune, Forte, Galderma, Incyte, Janssen, Landos, LEO Pharma, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma and UCB Pharma.

RBW: Consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis and UCB Pharma; honoraria from Astellas, DiCE, GSK and Union.

DdC, CM, VV: Employees and shareholders of UCB Pharma.

MW: Employee of UCB Pharma.

KAP: Received honoraria and/or grants from AbbVie, Akros, Amgen, Anacor, Arcutis, Astellas, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Canfite, Celgene, Coherus, Dermira, DiCE, Dow Pharma, Eli Lilly, Evelo, Galapagos, Galderma, Genentech, Gilead, GSK, Janssen, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, MedImmune, Merck (MSD), Merck-Serono, Mitsubishi Tanabe Pharma, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron,Roche, Sanofi-Aventis/Genzyme, Sun Pharma, Takeda, UCB Pharma and Valeant/Bausch Health.

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49. Bimekizumab Efficacy in High-impact Areas for Patients with Moderate to Severe Plaque Psoriasis: Pooled Results through 48 Weeks from the BE SURE and BE RADIANT Phase 3 Trials

Joseph F. Merola,[1] Alexa Kimball,[2] Yayoi Tada,[3] Jose-Manuel Carrascosa,[4] Boni Elewski,[5] Luke Peterson,[6] Christopher Cioffi,6 Natalie Nunez Gomez,[7] Valerie Ciaravino,[8] Ulrich Mrowietz[9]

[1]Brigham and Women's Hospital, MA, USA; [2]Beth Israel Deaconess Medical Center and Harvard Medical School, MA, USA; [3]Teikyo University School of Medicine, Tokyo, Japan; [4]Institute for Health Science Research Germans Trias i Pujol, Barcelona, Spain; [5]University Hospitals of Cleveland, Case Western Reserve University, OH, USA; [6]UCB Pharma, NC, USA; [7]UCB Pharma, Belgium; [8]UCB Pharma, France; [9]University Medical Center Schleswig-Holstein, Campus Kiel, Germany

Introduction: Psoriasis affecting the scalp, nails, palms and soles can cause physical impairment and negatively impact quality of life; management of psoriasis in these high impact areas poses a challenge for physicians and patients. We report scalp, nail and palmoplantar outcomes over 48 weeks (wks) from two bimekizumab (BKZ) phase 3 trials in plaque psoriasis, investigating two different maintenance dosing regimens.

Methods: Data were pooled for patients with moderate to severe plaque psoriasis from BE RADIANT (NCT03536884) and BE SURE (NCT03412747), who were randomized at baseline to receive BKZ 320mg every 4 wks (Q4W) to Wk16, and then either continued to receive BKZ Q4W (Q4W/Q4W) or switched to BKZ 320mg every 8 wks (Q4W/Q8W) in the maintenance period.

Patients included in these analyses had regional psoriasis involvement at baseline: scalp Investigator's Global Assessment (IGA)≥3 (5-point scale [0–4]), modified Nail Psoriasis Severity Index (mNAPSI)>10 (total fingernail score on a 0–130 scale), or palmoplantar (pp)-IGA≥3 (5-point scale [0–4]). Proportions of patients who achieved complete regional clearance (scalp IGA0, mNAPSI0, pp IGA0) are reported to Wk48. Missing data were imputed as non-response.

Results: Overall, 300 and 369 patients received BKZ Q4W/Q4W and BKZ Q4W/Q8W, respectively. Of these patients, 237 (79.0%) and 261 (70.7%) had scalp IGA≥3; 94 (31.3%) and 121 (32.8%) had mNAPSI>10; 56 (18.7%) and 50 (13.6%) had pp IGA≥3, at baseline.

Among patients who had scalp IGA≥3 at baseline, 80.2% and 82.0% treated with BKZ Q4W/Q4W and Q4W/Q8W achieved scalp IGA0 at Wk16, respectively. Of the patients who had pp IGA≥3 at baseline, 73.2% and 80.0% treated with BKZ Q4W/Q4W and Q4W/Q8W achieved pp-IGA0 at Wk16, respectively. Scalp IGA0 and pp-IGA0 responses were maintained to Wk48 with BKZ Q4W or Q8W maintenance dosing.

Of the patients with baseline mNAPSI>10, 20.2% and 26.4% treated with BKZ Q4W/Q4W and Q4W/Q8W achieved mNAPSI0 at Wk16, respectively. The percentage of patients who achieved mNAPSI0 increased during the trials; 59.6% of patients receiving BKZ Q4W/Q4W and 65.3% of patients receiving BKZ Q4W/Q8W achieved mNAPSI0 at Wk48.

Conclusion: Complete clearance of scalp and palmoplantar psoriasis was achieved by a high percentage of BKZ-treated patients at Wk16, with responses sustained to Wk48. Complete nail clearance increased from Wk16 to Wk48, reflective of the longer timescale required for nail growth and repair. Regional clearance was comparable between BKZ Q4W and Q8W maintenance dosing regimens.

Funding: UCB Pharma.

Disclosures:

JFM: Consultant for AbbVie, Amgen, Bayer, Biogen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi-Regeneron, and UCB Pharma; principal investigator for Dermavant, LEO Pharma, and UCB Pharma.

AK: Consultant and investigator for AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, LEO Pharma, Meiji Pharma, Novartis, Pfizer, Regeneron, and UCB Pharma; advisor to the Organization of Teratology Information Services (OTIS) and Ventxy Biosciences; fellowship funding from AbbVie and Janssen; Board of Directors: Almirall.

YT: Honoraria and/or grants from AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Eisai, Eli Lilly, Janssen, Kyowa Hakko Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Sun Pharma, Taiho Pharmaceutical, Torii Pharmaceutical, and UCB Pharma.

JMC: Principal/senior investigator and/or consultant

and/or advisor for AbbVie, Amgen, Biogen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Sandoz, and UCB Pharma.

BE: Research support as funding to Case Western Reserve University from AbbVie, AnaptysBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Incyte, LEO Pharma, Merck, Menlo, Novartis, Pfizer, Regeneron, Sun Pharma, Valeant, and Vanda; consultant (honoraria) from Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, LEO Pharma, Menlo, Novartis, Pfizer, Sun Pharma, UCB Pharma, Valeant, and Verrica.

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50. Bimekizumab Response Maintenance through Two Years of Treatment in Patients with Moderate to Severe Plaque Psoriasis Who Responded After 16 Weeks: Interim Results from the BE BRIGHT Open-label Extension Trial

Bruce Strober,[1,2] Akihiko Asahina,[3] Ulrich Mrowietz,[4] Mark Lebwohl,[5] Peter Foley,[6] Richard G. Langley,[7] Jonathan Barker,[8] Christopher Cioffi,[9] Nancy Cross,[9] Maggie Wang,[9] Carle Paul[10]

[1]Yale University, New Haven, Connecticut, USA; [2]Central Connecticut Dermatology Research, Cromwell, Connecticut, USA; [3]Department of Dermatology, The Jikei University School of Medicine, Tokyo, Japan; [4]Psoriasis-Center, Department of Dermatology, University Medical Center Schleswig-Holstein, Campus Kiel, Germany; [5]Icahn School of Medicine at Mount Sinai, New York, New York, USA; [6]The University of Melbourne, St. Vincent's Hospital Melbourne, Fitzroy and Probity Medical Research Inc., Skin Health Institute, Carlton, Victoria, Australia; [7]Division of Clinical Dermatology and Cutaneous Science, Dalhousie University, Halifax, Nova Scotia, Canada; [8]St John's Institute of Dermatology, King's College London, London, UK; [9]UCB Pharma, Raleigh, North Carolina, USA; [10]Toulouse University and CHU, Toulouse, France

Introduction: Plaque psoriasis is a chronic disease; it is important to understand long-term treatment efficacy.

Methods: Patients who completed one of three phase 3 studies could enroll in the BE BRIGHT (NCT03598790) two-year open-label extension (OLE).[1–3] These analyses include patients randomized to bimekizumab (BKZ) 320mg every 4 weeks (wks; Q4W) who responded at Wk16 of the feeder study, received BKZ 320mg Q4W or every 8 wks (Q8W) maintenance dosing from Wk16, and enrolled in BE BRIGHT.

We report maintenance of IGA0/1, BSA≤1% and PASI100 (complete skin clearance) through two years of treatment (OLE Wk48) among Wk16 responders who received continuous BKZ maintenance dosing in the OLE (Q4W/Q4W/Q4W or Q4W/Q8W/Q8W). Missing data were imputed using modified non-responder imputation (mNRI): patients with missing data following treatment discontinuation due to lack of efficacy were considered non responders; multiple imputation methodology was used for other missing data. Wk16 responder rates (NRI) are included for context.

Results: 989 patients were initially randomized to BKZ Q4W; at Wk16, 87.5% achieved IGA0/1; 74.9% achieved BSA≤1%; 62.7% achieved PASI100 (NRI).

Among Wk16 IGA0/1 responders, 93.9% (Q4W/Q4W/Q4W; n=384) and 97.8% (Q4W/Q8W/Q8W; n=185) maintained IGA0/1 to OLE Wk48. Among Wk16 BSA≤1% responders, 90.7% (Q4W/Q4W/Q4W; n=330) and 92.5% (Q4W/Q8W/Q8W; n=172) maintained BSA≤1% to OLE Wk48. Among Wk16 PASI100 responders, 83.7% (Q4W/Q4W/Q4W; n=275) and 86.3% (Q4W/Q8W/Q8W; n=147) maintained PASI100 to OLE Wk48.

Conclusion: A high proportion of patients who achieved complete or near complete skin clearance after 16 wks of BKZ treatment maintained responses through to two years with continuous Q4W or Q8W maintenance dosing.

References:

1. Reich K. Lancet 2021;397:487–98; 2. Gordon KB. Lancet 2021;397:475–86; 3. Warren RB. N Eng J Med 2021;130–41.

Funding: UCB Pharma.

Disclosures:

BS: Consultant (honoraria) from AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Equillium, GSK, Janssen, LEO Pharma, Meiji Seika Pharma, Mindera, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB Pharma; speaker for AbbVie, Amgen, Eli Lilly, Janssen, and Ortho Dermatologics; Scientific Director (consulting fee) for CorEvitas Psoriasis Registry; investigator for AbbVie, Cara Therapeutics, CorEvitas Psoriasis Registry, Dermavant, Dermira, and Novartis; Editor-in-Chief (honorarium) for Journal of Psoriasis and Psoriatic Arthritis.

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ML: Employee of Mount Sinai and receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen, Ortho Dermatologics, Regeneron, and UCB Pharma; consultant for Aditum Bio, AnaptysBio, Almirall, Arcutis, Aristea, Arrive Technology, Avotres, BioMx, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant, Dr. Reddy's Laboratories, Evelo, Evommune, Facilitate International Dermatologic Education, Forte, Foundation for Research and Education in Dermatology, Helsinn, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, and Verrica.

PF: Grant support from AbbVie, Amgen, Celgene, Eli Lilly, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Sanofi,

and Sun Pharma; served as an investigator for AbbVie, Akaal, Amgen, Arcutis, Aslan, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Eli Lilly, Galderma, Geneseq, Genentech, GSK, Hexima, Janssen, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma, and Valeant; served on advisory boards for AbbVie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Mayne Pharma, Merck, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Valeant; served as a consultant for Bristol Myers Squibb, Eli Lilly, Galderma, Janssen, LEO Pharma, Mayne Pharma, MedImmune, Novartis, Pfizer, Roche, UCB Pharma, and Wintermute; received travel grants from AbbVie, Eli Lilly, Galderma, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Roche, Sun Pharma, and Sanofi; served as a speaker for or received honoraria from AbbVie, Amgen, Celgene, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Roche, Sanofi, Sun Pharma, and Valeant.

RGL: Principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma; provided lectures for AbbVie, Amgen, Celgene, LEO Pharma, Merck, Novartis, and Pfizer.

JB: Attended advisory boards and/or received consultancy fees and/or spoken at sponsored symposia and/or received grant funding from AbbVie, Almirall, Amgen, AnaptysBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Samsung, Sienna, Sun Pharma, and UCB Pharma.

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51. Bimekizumab Safety in Patients with Moderate to Severe Plaque Psoriasis: Analysis of Pooled Data from Up to Two Years of Treatment in Phase 2 and 3 Clinical Trials

Kristian Reich,[1] Mona Ståhle,[2] Yukari Okubo,[3] Linda Stein Gold,[4] Joseph F. Merola,[5] Luke Peterson,[6] Krista Wixted,[6] Nancy Cross,[6] Delphine Deherder,[7] Richard Langley[8]

[1]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [2]Karolinska Institutet, Stockholm, Sweden; [3]Tokyo Medical University, Tokyo, Japan; [4]Henry Ford Health System, MI, USA; [5]Brigham and Women's Hospital, MA, USA; [6]UCB Pharma, NC, USA; [7]UCB Pharma, Belgium; [8]Dalhousie University, Nova Scotia, Canada

Introduction: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A. Here, we report long-term safety data in BKZ-treated patients with moderate to severe plaque psoriasis pooled to include two years of treatment from phase 2 and 3 clinical trials.

Methods: Long-term safety was evaluated for patients who received ≥1 dose of BKZ in four phase 3 (BE SURE, BE VIVID, BE READY, and their open-label extension [OLE] BE BRIGHT; data cut-off: 9 Nov 2020) and four phase 2 (BE ABLE 1, BE ABLE 2, PS0016, PS0018) trials. Safety data were also evaluated separately for patients who received BKZ 320mg Q4W or Q8W in phase 3 trials only. Treatment-emergent adverse events (TEAEs) were coded using MedDRA v19.0. Exposure-adjusted incidence rates (EAIRs), incidences of new cases per 100 patient-years (PY), are presented.

Results: Total BKZ exposure was 3109.7PY (N=1789) across the phase 2/3 trials and in phase 3 was 2740.8PY (N=1495) (Q4W: 1863.6PY, N=1456; Q8W: 879.8PY, N=930). TEAEs occurred at a rate of 202.4/100PY across the phase 2/3 trials, serious TEAEs at 5.9/100PY, and TEAEs leading to discontinuation at 3.8/100PY. Eleven deaths occurred, with an EAIR of 0.4/100PY; none were considered related to study treatment. TEAEs were less frequent in BKZ Q8W- vs BKZ Q4W-treated patients. The most common TEAEs in the phase 2/3 trials with BKZ were nasopharyngitis, oral candidiasis, and upper respiratory tract infection, at 19.1, 12.6, and 8.9/100PY, respectively.

Serious infections (1.0/100PY) were less frequent in BKZ Q8W-treated patients vs Q4W-treated patients. There were no cases of active tuberculosis or serious COVID-19. The EAIR of oral candidiasis (12.6/100PY) decreased vs one year of BKZ treatment (16.4/100PY), and was lower with BKZ Q8W (9.6/100PY) than with Q4W (16.4/100PY). No serious oral candidiasis events occurred; most were mild/moderate (98.5% experiencing oral candidiasis) and rarely led to study discontinuation (0.9% of patients experiencing oral candidiasis). EAIRs for inflammatory bowel disease (0.1/100PY), adjudicated major adverse cardiac events (0.5/100PY) and malignancies (0.8/100PY) were low and as expected for the plaque psoriasis population. There was one adjudicated suicidal ideation/behavior event in a BKZ Q4W-treated patient.

Conclusion: BKZ was well tolerated; no new safety signals were identified over two years of treatment. EAIRs of TEAEs and TEAEs of interest, including oral candida infections, were generally lower in patients receiving BKZ Q8W vs BKZ Q4W and did not increase with longer duration of BKZ exposure as compared with one year of BKZ treatment.

Funding: UCB Pharma.

Disclosures:

KR: Served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Affibody, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, Centocor, Covagen, Eli Lilly, Forward Pharma, Fresenius Medical Care, Galapagos, Galderma, GSK, Janssen, Kyowa Kirin, LEO Pharma, Medac, MSD, Miltenyi Biotec, Novartis, Ocean Pharma, Pfizer, Samsung Bioepis, Sanofi, Sun Pharma, Takeda, UCB Pharma, Valeant/Bausch Health, and Xenoport.

MS: Received honoraria for participating in advisory boards and has given lectures for AbbVie, Celgene, Eli Lilly, LEO Pharma, Lipidor, Novartis, Pfizer, and UCB Pharma.

YO: Research grants from Eisai, Maruho, Shiseido, and

Torii Pharmaceutical; current consulting/advisory board agreements and/or speakers bureau and/or clinical trials from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eisai, Eli Lilly, Janssen, Jimro, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Pharma, Novartis, Pfizer, Sanofi Genzyme, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, and UCB Pharma.

LSG: Consultant for AbbVie, Amgen, Arcutis, Dermavant, LEO Pharma, Bristol Myers Squibb, Eli Lilly, Novartis, Pfizer, Sanofi-Regeneron, and UCB Pharma; principal investigator for AbbVie, Arcutis, Dermavant, LEO Pharma, Novartis, and UCB Pharma.

JFM: Consultant for AbbVie, Amgen, Bayer, Biogen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi-Regeneron, and UCB Pharma; principal investigator for Dermavant, LEO Pharma, and UCB Pharma.

LP, KW, NC: Employees and shareholders of UCB Pharma.

DD: Employee of UCB Pharma.

RL: Principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma; provided lectures for AbbVie, Amgen, Celgene, LEO Pharma, Merck, Novartis, and Pfizer.

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The official journal of the Society of Dermatology Physician Assistants

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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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In a post-quarantine world, patients struggling with acne flare ups might feel like they're still missing out on life. Now is the time to discuss the latest science-based solutions in acne with your patients. Don't let acne hold them back, include acne assessments in student annual physicals.

You can help patients overcome the barriers of facial and truncal acne. Galderma is committed to innovation in skin health. Explore our latest innovation in acne treatment.

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