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TABLE OF **CONTENTS**

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The Necessity to Adapt during COVID-19 Crisis Sparks Innovation, Growth, Development

At the beginning of 2020, I joined the editorial team of *Journal of Dermatology for Physician Assistants (JDPA)* as a deputy editor, a position I accepted with great honor and enthusiasm. After all, the start of a new year is an ideal time to embark on new journeys and embrace change. As I settled into my new role with *JDPA*, we discussed our goals for the year ahead—to provide quality, peer-reviewed content for the derm PA readership and to highlight the unique experiences, achievements, and insights of providers and patients alike. In addition to the scientific research, we wanted to cover the human aspect of the derm PA profession; to share the personal stories of those making an impact on others and discuss observations being made in practices across the country. One unifying, albeit initially terrifying, experience in 2020 for all of us has been the COVID-19 pandemic, which has had far-reaching impacts within all realms of our clinical practice, professional associations, and personal lives. While time continues to pass and we learn more about this virus that has turned our lives upside down, we continue to see innovation rise from the necessity to adapt.

In response to COVID-19 we have seen virtually everything go, well, virtual. Healthcare providers swiftly enacted telemedicine, which gave patients the opportunity to be "seen" without having to physically come into the office. While this offering filled a practice gap in a time of great need, adapting to telemedicine, particularly teledermatology, has presented its own set of challenges. First, flipping the virtual switch likely illuminated technical difficulties for many of us; poor internet connections causing delays in video and audio, disruption in the flow of appointment schedules, and perhaps the most frustrating, limitations in providing care virtually in a specialty that is highly visual and hands on.

Dermatology, both in the clinical and aesthetic settings, is also procedurally based. With in-person visits and procedures only being performed in emergent derm cases, clinical practices were forced to put scheduled procedures on hold and predominately aesthetic based practices halted anything that was deemed non-essential (i.e., cosmetics). A slowing or complete stop to in-person practice meant decreased workload, which immediately translated to decreased hours and salary/compensation or furlough for many clinicians. During the height of the pandemic, all areas of healthcare seemed to be operating at bare-bone capacity, hoping to ride out an invisible storm with an unpredictable future.

These are just a few of the obstacles encountered by dermatology PAs during these unprecedented times. While COVID-19 is still an enigma to most of us, some have encountered it head on and witnessed its devastation. Some of our very own derm PAs adapted to the disruption in their professional lives and answered the call to serve where they were most needed—on the front lines of the nation's pandemic epicenters of New York, New York, and Seattle, Washington. In this issue, we share some of their stories.

I am certain I am not alone in feeling sheer annoyance in response to such rapid changes. Although frustration abounds change, this year has proven to be a time of growth and development. I appreciate all those who have stepped out of the box to continue to provide patient care, education, and services during this time. I look forward to the days when we can meet in-person for education and fellowship, with or without our masks and hand sanitizer! I don't know how much "pandemic life" will follow us into 2021, but I do know that the grit and innovation we've shown this year will carry us into the uncertain future.

I hope you enjoy this latest issue.

Regards,

Joleen M. Volz

Joleen M. Volz, DMSc, PA-C, DFAAPA
JDPA Deputy Editor
jdpa@dermpa.org

Crafting a Solution–Adapting to Meet the Challenges of an Ongoing PPE Crisis

As the COVID-19 pandemic surged, many people looked for ways in which they could be productive and even help with crisis response. A solution was found in an unlikely market—Arts and Crafts. Social media circles and the Centers for Disease Control and Prevention (CDC), encouraging the use of homemade face masks to help prevent the spread of the virus, began posting step-by-step instructions and tutorial videos on do-it-yourself mask making. Calls for homemade items, such as face masks, suddenly abounded the internet.

Although the dire need for homemade face masks has largely subsided, the United States is still facing serious personal protective equipment (PPE) shortages in many parts of the nation. Get Us PPE, a grassroots movement founded by emergency physicians on the front lines of the COVID-19 pandemic and driven by volunteers across the country, has received more than 16,000 registered requests for PPE to date. Through a coalition of data scientists, makers, partners, and donors, Get Us PPE has amassed the largest non-governmental database of PPE shortages in the United States. According to the most recent data report from Get Us PPE,[1] the most in-demand types of PPE (indicated by requests received) were as follows:

#1-Gowns
#2-Masks (Surgical/Procedure)
#3-Filtering Facepiece Respirators
#4-Disinfecting Wipes
#5-Face Shields

The report also shows that demand for these items has varied by state and even fluctuated likely based on changing needs. For example, the most requested type of PPE in Florida has been filtering facepiece respirators (N95s and equivalent) every month since April. Request data from facilities in New York state showed most in-demand items changed from respirators in April, May, and June 2020 to disinfecting wipes beginning with July 2020.

1. Get Us PPE. Shortage Index August 2020. https://v9b3g8f2.stackpathcdn.com/wp-content/uploads/2020/09/Get-Us-PPE-Data-Shortage-Index-August-2020.pdf. Accessed October 5, 2020.

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PA Personality

JDPA Deputy Editor, SDPA Past President Joleen M. Volz, DMSc, PA-C, DFAAPA, Shows Her Creativity for the PPE Cause

"I never really considered myself to be much of a crafter. When my kids were young, I made their Halloween costumes. Then, about eight years ago, I traded my average sewing machine for a fancy one that could also embroider. My sister, who works as a nurse in an intensive care unit, relayed the great need for more face coverings, so I knew that anything, even homemade, was better than nothing. When I saw the mask design, it looked simple enough, so I decided to try my hand at making a few basic ones. Once that seemed to be successful, I got a little more creative with the material and embroidery, putting some personal touches on ones for family, friends, and coworkers. I found that the greatest challenge in making the masks wasn't a lack of time, but rather lack of materials since people all over the world were dusting off their sewing machines."

Joleen M. Volz, DMSc, PA-C, DFAAPA

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.

Society of Dermatology Physician Assistants Annual Fall Dermatology Conference––SDPA Digital 2020
Virtual, Live Dates:
October 29-November 1, 2020
https://sdpadigital.org/

Skin Disease Education Foundation's (SDEF) 16th Annual Women's & Pediatric Dermatology Seminar
Virtual, Live Dates: December 11-12, 2020
https://www.globalacademycme.com/conferences/sdefs-annual-womens-pediatric-dermatology/welcome-sdefs-16th-annual-womens-pediatric

American Academy of Dermatology (AAD) 79th Annual Meeting
March 19-23, 2021
San Francisco, California
https://www.aad.org/

Society for Investigative Dermatology Annual Meeting
May 5-8, 2021
Chicago, Illinois
https://www.sidnet.org/

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

FROM THE PRESIDENT'S DESK:

"SDPA Digital" 100-percent Live, Virtual Conference Represents Just One Example of Embracing Inevitable Changes in 2020

Dear Colleagues,

As we enter a new season, I can't help but notice that with the COVID-19 pandemic still lingering, fall 2020 looks strange and a little unfamiliar. Typically, we would be welcoming fall with the beginning of the school year (in person) in September, settling into new schedules and habits that naturally follow the tell-tale signs of fall and winter we all recognize. The weather gets a little colder. Daylight, though present through the tree's changing leaves, doesn't last as long as it did during the seemingly endless summer, and our nights are increasingly spent indoors.

This year, we know fall is here, and yet we are also aware that nearly everything is different. The most obvious routine that we have seen upended is school, but there are other changes taking place. We have all made adjustments in our personal and professional lives to account for the pandemic's impact, and although we largely have no control over when change is demanded from us, we do have control in how we approach that change. When faced with inevitable change and challenges in life, we all have a choice to make about whether we will embrace or resist.

Confronted with all the changes and subsequent challenges presented this year, the Society of Dermatology Physician Assistants (SDPA) has chosen the former choice—to embrace. Over the summer, we evaluated the current and potential course of COVID-19 and made the difficult but necessary decision to change the format of the SDPA Fall 2020 Conference from an in-person event (planned to take place in Miami, Florida) to a 100-percent live, virtual format called SDPA Digital. Collectively, the SDPA Board of Directors felt this was the best decision to ensure the health and safety of everyone who would be in attendance. The SDPA has always prided itself on excellence, and SDPA Digital 2020 will be no exception. Society staff and leaders have worked overtime to make sure this virtual experience is as engaging as it is educational. I hope to "see" each and everyone one of you there. SDPA Digital is only one example of the many ways SDPA has embraced the challenges of COVID-19. I look forward to sharing some other great initiatives we have in the works as more details are released.

So, as we settle into fall, I ask each of you to reflect on your response to the following question, "When faced with inevitable change and challenges in my life, do I choose to embrace or resist them?" It's never too late to change our responses for the better. As the saying goes, "We don't grow when things are easy, we grow when we face challenges." I will be reflecting alongside you and logging on to SDPA Digital 2020 as I sip on what has become a much-anticipated fall favorite—yes, a pumpkin spice latte! I guess COVID-19 hasn't changed all of our fall traditions.

With you and for you,

Archana M. Sangha, MMS, PA-C
President SDPA

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The Dermatology Physician Assistant's Role in Recognizing and Treating Psoriasis-associated Depression

By Laura Bush, DMSc, PA-C, DFAAPA

ABSTRACT

The purpose of the article is to explain the role of inflammation in psoriasis and its connection to comorbid depression, expand on recognition of depression in psoriasis patients, and explain efficient screening tools, diagnosis, and treatment options for physician assistants

KEYWORDS

Psoriasis, depression, comorbidity, autoimmune, proinflammatory, cytokines

» CME

This program has been reviewed and is approved for a maximum of .5 hours of AAPA Category I CME credit by the Physician Assistant Review Panel.

Approval is valid for 1 year from the issue date of October 26, 2020. Participants may submit the self-assessment exam at any time during that period.

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SDPA members may access the post-test at https://www.dermpa.org/JDPA_Exams

Learning Objectives:

1. ***Describe** the pathophysiology of psoriasis and how the inflammatory process seen in patients with psoriasis may also contribute to comorbidities such as depression.*
2. ***Summarize** available screening tools designed to help healthcare providers determine if a patient is suffering from depression and list considerations in implementing these into practice.*
3. ***Discuss** available treatment options that support treating psoriasis and depression concurrently*

INTRODUCTION

Psoriasis is a chronic, autoimmune systemic disease affecting roughly 7.5 million people in the United States and more than 125 million worldwide.[1-3] Although psoriasis is visualized externally, it is important that healthcare providers are educated on internal processes that contribute to the inflammatory state seen in patients with psoriasis as well as known psoriasis-related comorbidities, such as depression.

Psoriasis can begin with a trigger or injury causing keratinocytes to respond by proliferating at an accelerated rate, causing neovascularization, and recruiting T cells which produce cytokines.[4] These cytokines are an active component in the inflammatory process and may play a significant role in associated comorbid conditions.[5-8] An elevation of proinflammatory cytokines exists in both psoriasis and depression.[5,7,9] Both this potential link with proinflammatory cytokines and the psychosocial effects of such a visible disease can result in the development of depression for those who have psoriasis.[3,7,9]

Depression, a comorbid condition of psoriasis, can lead to overall adverse health, impacting sleep, sexual function, and increased psychiatric morbidity and mortality.[3,8,10,11] Depression can also be associated with anxiety, and possibly give rise to suicidal ideation or suicide.[7] Depression associated with psoriasis warrants recognition, screening, diagnosis, treatment, and prevention. Comorbid depression is often under-diagnosed because of a lack of screening and awareness. Without adequate resources, knowledge of available screening tools, and straightforward treatment guidelines, the dermatology clinician caring for patients with psoriasis might face challenges in diagnosing and treating comorbid depression. Streamlining the process of recognizing depression will equip the busy clinician with efficient options for evaluation and treatment.

PATHOPHYSIOLOGY

Although psoriasis is common, there is still much to learn about the cause, pathophysiology, methods to

evaluate, and treatment of associated conditions. Psoriasis appears to begin with a stressor that causes an increase in tumor necrosis factor-α (TNF-α), a signaling protein, and release of cytokines Interleukin (IL)-6, IL-12, and IL-23 that activate the naïve T cells to convert to T helper 1 cells (TH-1) and TH-17.[4,5,7,9] This cascade causes a release of IL-17 and interferon-ɣ, stimulating rapid keratinocyte proliferation and a flood of immune cells.[4,7] The result is an inflamed, thick psoriasis plaque. Although not proven, cytokines and the inflammatory process may play a role in the association of depression and psoriasis.[7,8]

TABLE 1. DEPRESSION SCREENING TOOLS

Screening tool	Number of questions	Time to complete	Administered by	Free/ Cost	Screens for suicide ideation
PHQ-2	2	<1 minute	Patient	Free	No
PHQ-9	9	<3 minutes	Patient	Free	Yes
PROMIS-D	21	1 minute	Patient	Free	No
HADS	14	5 to 7 minutes	Provider	Cost	No
BDI-II	21	15 minutes	Provider	Cost	No

Abbreviations: PHQ: Patient Health Questionnaire; PROMIS-D: Patient-reported Outcomes Measurement Information System-Depression; HADS: Hospital Anxiety and Depression Scale; BDI-II: Beck Depression Inventory-Second Edition

SCREENING FOR DEPRESSION IN PATIENTS WITH PSORIASIS

Psoriasis-associated depression often goes unrecognized and untreated, which can negatively affect patients. One systematic review and meta-analysis study found that 28 percent of psoriasis patients had symptoms of depression, while 12 percent had clinical depression.[12] If clinicians have neither formal psychological training nor expanded knowledge of depression symptoms and treatment, addressing a patient's mental health state might be uncomfortable for clinician and patient alike.[13] Having a quick and simple screening tool available may make the process of screening for depression easier for both the provider and the patient. Screening tools help determine if a patient is suffering from depression and monitor their improvement in treatment. Several easy-to-use options for screening are readily available in print or as computer-generated tools.

The Patient Health Questionnaire. The Patient Health Questionnaire (PHQ) has credible reliability and validity in screening for depression.[10,11,14,15] One version of the PHQ, the PHQ-9, demonstrates high validity (area under receiver operating characteristic curve [AUROC] 0.85, 95% confidence interval [CI] 0.82-0.88]) with 49 percent sensitivity and 94 percent specificity.[15] At the same time, the PHQ-2 was also valid (AUROC 0.76, 95% CI 0.73-0.79), although to a lesser degree, with sensitivity 60 percent and specificity 84 percent.[15] In comparison, the PHQ-2 has only two questions, while the PHQ-9 is more comprehensive with nine questions.[15] The PHQ-2 has the advantage of being very quick to complete.[15,16] However, if positive, the patient may be given the PHQ-9 for confirmation.

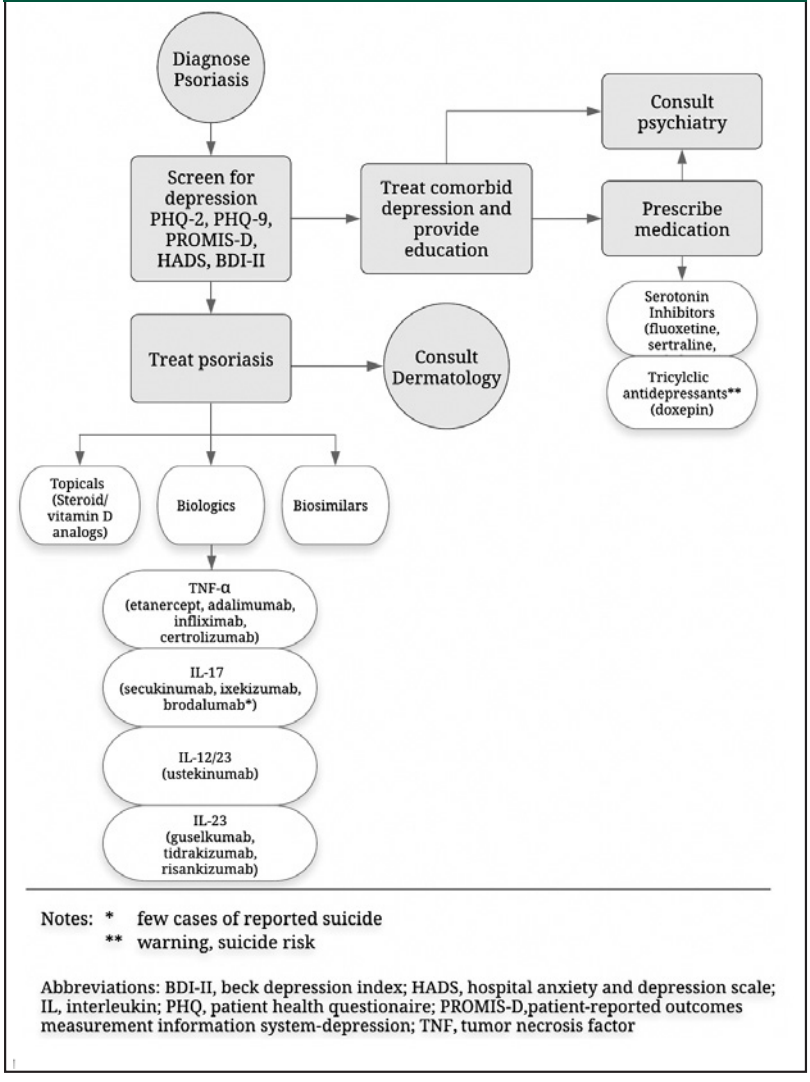
The Patient-Reported Outcomes Measurement Information System-Depression. The Patient-Reported Outcomes Measurement Information System-Depression (PROMIS-D) developed by the National Institutes of Health (NIH), is patient-reported. In a recent article published in the *British Journal of Dermatology*, Gaufin et al found that the PROMIS-D was significantly better at identification than PHQ-9 ($p<0.01$).[16] In comparison, the PROMIS-D is longer than the PHQ-9 but can be done at home and has a built-in system to flag patients screening positive for moderate to severe depression.[16] Every practice is different; factors to consider might be location, language barriers, and time available when choosing the right screening tool. PROMIS-D is advantageous as it is reliable, convenient, and accessible in many languages.[16] It is patient-reported electronically; therefore, the PROMIS-D can be done at home and integrated digitally into a patient's chart.[16]

Other Tools and Considerations for Use. The Hospital Anxiety and Depression Scale (HADS) is frequently used in research but would not be as useful in a dermatology care setting because it is provider-driven and has associated costs to administer. The Beck Depression Inventory-Second Edition (BDI-II), with sensitivity 88 percent and specificity 92.1 percent, is a valid and reliable tool comparable to the PHQ-9, but the PHQ-9 is free, shorter, and easier to use.[13,14] Therefore, a reasonable choice would be a printed PHQ-2, PHQ-9, or an electronic PROMIS-D, which are all patient-driven. It is best to have a consistent procedure for evaluation and follow up with whichever screening tool is used. The screening tools are summarized in *Table 1.*

TREATING PSORIASIS FROM THE INSIDE OUT

The treatment options for psoriasis have grown and

FIGURE 1. FLOWCHART FOR DEPRESSION SCREENING AND TREATMENT IN PATIENTS WITH PSORIASIS



improved over the past decade. In dermatology, we often appropriately reach for a topical steroid or a vitamin D analog to treat the skin; however, when considering inflammation-driven comorbidities, drug choice should focus on the internal process of psoriasis. Patients' skin often flares when under stress, supporting treatment of both psoriasis and depression concurrently.[17]

Biologics. Multiple studies report the improvement of depression using biologic therapies.[8,17] TNF inhibitors and IL-12/23 blockers have shown to improve depression in several randomized controlled studies.[8,17,18] This improvement may be partially due to the biologics targeting the inflammatory cytokines resulting in skin clearance, leading to improved self-image and quality of life.[8,9,17,18]

TNF inhibitors. The TNF inhibitors are a class of biologic medication that block TNF-α.[19] These include etanercept, adalimumab, infliximab, and certolizumab.[19] They were often first-line agents in psoriasis unless otherwise contraindicated, however, as more treatment options are available, this is changing. Most research on treatment with biologics has been with the anti--TNF-α. Etanercept, adalimumab, and a small case study on infliximab all show improvement in psoriasis and depressive symptoms.[8,17-19]

IL-12/23, IL-17, and IL-23. The next biologic proven to be effective in treating moderate-severe psoriasis as well as decreasing comorbid depressive symptoms is ustekinumab, an IL-12/23 blocker.[8,10,18,19] High IL-17 levels are present in patients with major depression.[9] Secukinumab, ixekizumab, and brodalumab are three available IL-17 blockers indicated for the treatment of psoriasis.[19] Because of observed suicidal behavior in subjects treated with brodalumab, it is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Given the potential risks and benefits of biologic use in patients with a history of depression and/or suicidal ideation or behavior, IL-17 blockers warrant further investigation in the treatment of psoriasis with comorbid depression.[9,19]

The newer IL-23 class, including guselkumab, tidrakizumab, and risankizumab, improve psoriasis, and although not studied in depression, could, in theory, result in improvement, from clearance of skin lesions and improved psychosocial implications.[19] When selecting a biologic, the provider must consider the patient's comorbidities and their overall medical condition.

Biosimilars. Biosimilars have recently become available as an alternative for many psoriasis biologic medications. They are complex proteins produced to be highly similar in function to traditional biologic medication.[20] Many steps are involved in the production of biosimilars, therefore, variations in manufacturing result in different biosimilar batches.[20] Each batch is unique but similar to other batches and other biologics.[20] Biosimilars are not identical copies of a biologic medication and are not considered generics.[20] Although not yet commonly used, these biosimilars will likely

become a popular and lower-cost option to traditional biologics for psoriasis treatment along with other autoimmune inflammatory disorders.

IDENTIFYING AND TREATING PATIENTS WITH PSORIASIS-ASSOCIATED DEPRESSION

Education. It is essential to discuss significant psoriasis comorbidities, including the elevated risk of anxiety and depression.[18] Patients might feel the stigma associated with depression or be unaware that they are experiencing depressive symptoms.[18] Thus, the use of a screening tool at this juncture can help the clinician identify those at risk for depression and provide an opportunity for treatment discussion, ultimately serving as a preventative measure. Once a patient is identified as having depressive symptoms, counseling, support groups, or referral to psychiatry may be warranted.[11,13] Several agents can also be considered for treating depression, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitor (SNRIs), or tricyclic antidepressants (TCAs).[11]

SSRIs. SSRIs are both effective and tolerable antidepressants, making them a favorable first choice, with fluoxetine and sertraline most commonly used.[11,13] Sertraline proved to be the best first option, starting at 50 mg each day and increasing 25 mg weekly if needed to a max dose of 200 mg daily.[13] Venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressant medication, is another option.[13]

TCAs. TCAs are one of the first classes of medication used to treat depression. When a patient's depressive symptoms center around itching and sleep disturbances, the tricyclic antidepressant doxepin is an option.[13] Doxepin dosing starts at 25 mg titrating up every week to 100 to 150 mg per day.[13] TCAs have a lethal dose, contradicting their use if any suicide risk exists.[13]

LIMITATIONS

At this time, the cytokine association with depression is theory. Future studies on the connection may lead to a better understanding of the association. Since current studies on psoriasis patients are not consistent in the screening instruments used to diagnose depression, a more standardized method in studying depression with consistent tools could yield a better comparison.

CONCLUSION

Psoriasis is a disease that encompasses more than what is visible on the skin. When caring for patients with psoriasis, it is equally important to consider what is happening inside along with outside the body. Treating the internal factors associated with the inflammation, as well as the outside factors, like the skin, is vital to the comprehensive care of patients with psoriasis. Dermatology physician assistants should educate patients on the association of depression with psoriasis, screen the patient with one of the available patient-driven screening tools, such as the PHQ-2, PHQ-9, or PROMIS-D, and observe them for any signs and symptoms of depression during the exam as patients often do not report symptoms because of fear or stigma. The inflammatory process as well as the psychosocial aspects of having psoriasis are implicated in depression.[5,7,8,13,18] Multiple studies favor using a biologic medication to manage psoriasis and depression with referral to psychiatry or adding antidepressant medicines if needed.[8,11,13,18] Recognizing comorbid depression and choosing the right treatment plan, including medication, counseling, and referrals, are essential to decreasing morbidity and mortality associated with psoriasis.

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Laura Bush, DMSc, PA-C, DFAAPA, *is a dermatology physician assistant at Fayette Area Dermatology in Fayetteville, Georgia. She is a graduate of Emory University in Atlanta, Georgia, and a recent graduate of the University of Lynchburg Doctor of Medical Science program in Lynchburg, Virginia. She has also served on the board of professional societies at both the state and national level.*

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

Address for correspondence: *laurapbush@yahoo.com*

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Disseminated Cryptococcus in a Solid Organ Transplant Patient

By Cynthia Faires Griffith, MPAS, PA-C

ABSTRACT

The presenting symptom for disseminated cryptococcal infection in a kidney transplant patient is new exophytic, cutaneous papules. Cryptococcosis is the third most common type of invasive fungal infection in organ transplant recipients. Cutaneous cryptococcus is the third most common presentation after meningitis and pulmonary involvement. This patient presented without fever, altered mental status, or shortness of breath but was found to have meningitis, cutaneous and pulmonary involvement at her time of presentation.

CASE DESCRIPTION

A 66-year old woman of Hispanic descent referred to the author's dermatology office for a work-in, acute visit for a new skin spot. She presented with multiple, pruritic papules on the left hairline, left cheek, right helix, chin, left forearm and right upper back. The patient was referred to dermatology by her kidney transplant physician assistant (PA), who expressed concern over the patient's new skin eruption. Fifteen months prior to presenting to dermatology, the patient had a kidney transplant for kidney failure, a complication from having type 2 diabetes mellitus (T2DM). During her dermatology visit, the patient stated that the first papule appeared on the left hairline three weeks prior and the other sites, which she described as pruritic but not painful, continue to appear with no resolution. Her current medication list included prednisone 5 mg daily, tacrolimus 2 mg twice daily, and mycophenolic acid 360 mg twice daily for post-transplant immunosuppression. She reported no occurrences of fever, chills, or vomiting.

PHYSICAL EXAMINATION

Upon physical examination, the patient had numerous dome-shaped papules with central hemorrhagic crusting on the right helix, left cheek, left forearm *(Figure 1)*. There were similar smaller, molluscum contagiosum-like papules with central dells and some with hemorrhagic crusting on the chin, left forearm, right upper back, and left hairline. No lesions were observed on the abdomen or legs. Patient was afebrile in clinic and appeared to be without altered mental status. She exhibited no shortness of breath, no headache, no neck stiffness, and no fevers.

DIAGNOSTIC TESTING

The lesion on the left cheek *(Figure 1)* was biopsied for tissue culture (acid fast bacilli, fungal and aerobic culture). The lesion on the right helix *(Figure 2)* was swabbed for viral culture to rule out herpes simplex virus (HSV). The lesion on the left forearm was punch biopsied for hematoxylin and eosin (H&E) staining. The H&E biopsy came back prior to the cultures showing cutaneous cryptococcus.

The patient was admitted to the hospital. Her blood cultures for histoplasmosis and blastomycosis and coccidiomycosis were negative. Serum cryptococcus antigen titers of 1: 4096 were found in the patient's blood. The patient's cerebral spinal fluid (CSF) from her first lumbar puncture showed 83 nucleated cells, protein 53, < 1 red blood count (RBC), Glucose 70. The cerebral spinal fluid (CSF) was positive for Cryptococcus neoformans with an antigen titer of 1:2048. Chest xray and computed tomography (CT) scan at the time of her admission to

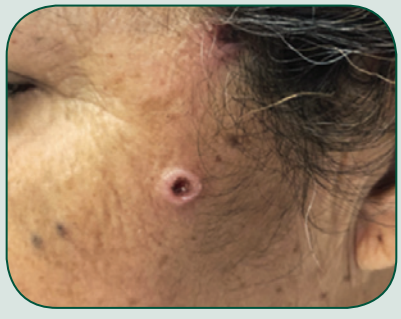

Figure 1: *Dome-shaped papule with hemorrhagic center of the left cheek.*

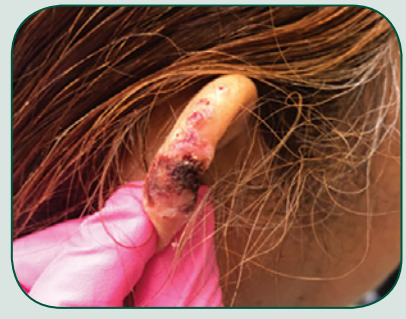

Figure 2: *Exophytic papule with a scalloped border and central hemorrhagic crusting on the right helix of the ear.*

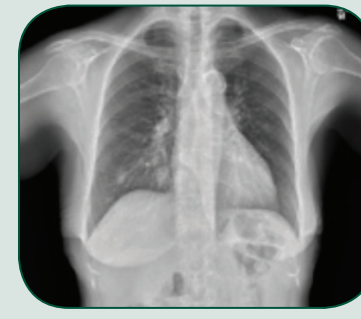

Figure 3: *Chest xray and computed tomography (CT) scan at the time of patient's admission to the hospital showing innumerable pulmonary nodules.*

the hospital showed innumerable pulmonary nodules *(Figure 3)*. Patient was diagnosed with disseminated cryptococci infection with lung, skin, and central nervous system (CNS) involvement. Brain CT and magnetic resonance imaging (MRI) showed no acute intracranial abnormalities.

DISCUSSION

Cryptococcosis is the third most common invasive fungal infection in solid organ transplant recipients (SOTRs) after Candida and Aspergillus[1]. The overall incidence of cryptococcus in SOTRs is 2.8 percent (range, 0.3%–5%),[2] with mortality rates reported between 33 and 42 percent.[3] Cryptococcal infection tends to present 16 to 21 months post-transplant,[1,2] the time of onset can be earlier typically less than 12 months in patients with liver or lung transplant.[4] This patient was 15 months post-transplant at the time of her presentation.

Cryptococcus is a fungus found in soil, decaying wood, and bird droppings. The two species of cryptococcus that are pathogenic are *Cryptococcus neoformans* and *Cryptococcus gattii*. *C. neoformans* causes most infections in SOTRs;[4] this is the species that was identified in our patient. This species has no predilection for a specific geographic region. *C. gatti* is typically thought to be a tropical fungus but it is now prevalent in the Pacific Northwest and British Columbia, Canada.[4] *C. gatti* is a reportable disease in Oregon and Washington.[4] Of note, endemic geographic maps of diseases like cryptococcus are being expanded due to climate change.

At time of presentation, the patient was living in Dallas, Texas. She was born in Mexico and moved to the United States when she was 15-years old. She previously lived in West Texas. She reported leaving Texas for a four-day trip to Florida four years prior to her transplant surgery. She was not involved in any unusual outdoor activities, such as gardening, camping, or hunting, where she might have been exposed to cryptococcus. She denied raw food consumption and exposure to farm animals or birds, another potential route of fungal infection. Diagnostic testing and further investigation did not lead to a definitive source or cause of the infection.

Cutaneous cryptococcus is the third most common presentation after meningitis and pulmonary involvement. Interestingly, our patient had involvement of all three of these body systems at her time of presentation. In addition, cryptococcus can affect the kidney. Evaluation of all these systems is important.

Cutaneous findings occur in 15 to 20 percent of disseminated cases. The presentation is variable. Cellulitis, abscesses, papules, plaques, ulcers, sinus tracts, or purpura may all be seen. In patients with human immunodeficiency virus (HIV), molluscum-like umbilicated papules are described. When left untreated, disseminated disease is fatal.

CONCLUSION

The patient was treated with amphotericin B 3 mg/kg administered intravenously (IV) and 5-fluorocytosine (5-FC) 1 gram four times daily. The patient had trouble tolerating the 5-FC at the prescribed dose; she experienced nausea and vomiting, so the care team recommended lowering the dose frequency to twice daily. She was treated with this antifungal combination for 23 days. CSF cultures on Day 11 were positive and thus she received extended doses of the amphotericin B and 5-FC. Repeat CSF culture on Day 16 was negative for cryptococcus. She was then switched to fluconazole 400 mg daily for eight weeks. Her tacrolimus dose was adjusted for the interaction with the fluconazole. At her outpatient follow up two weeks after completing treatment, her cutaneous lesions were beginning to resolve. She underwent continued lumbar punctures to monitor her CSF until it was clear of disease. Patient made a complete recovery.

CLINICAL ASIDE

The patient never had a fever and only reported experiencing mild neck pain and headache while in the hospital. She also did not exhibit mental status changes or any neurological symptoms. This subtle presentation is likely because her body could not mount an immune response to the cryptococcus infection because she was immunosuppressed from undergoing a kidney transplant. The first diagnostic tests to come back positive for the identifying the culprit fungus was the tissue H&E. The dermatopathologist saw the organism in tissue prior to other culture testing growing the organism. This was helpful in starting early targeted treatment.

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Cynthia Faires Griffith, MPAS, PA-C, *is a Dermatology Physician Assistant at UT Southwestern Medical Center in Dallas, Texas, where she also earned her Masters of Physician Assistant Studies. Ms. Griffith is the co-founder of the UT Southwestern High-Risk Skin Cancer Transplant Clinic, a twice-monthly clinical initiative to serve patients who are immunosuppressed after solid organ or bone marrow transplant. She also practices general adult medical dermatology. She is Dermatology Grand Rounds Department Editor for the Journal of Dermatology for Physician Assistants (JDPA) and is a guest lecturer in the UT Southwestern PA program and a lecturer at local, regional, and national conferences. She is a member of the Texas Academy of Physician Assistants, the Society for Dermatology Physician Assistants, and the American Academy of Physician Assistants. She was awarded UT Southwestern's PA of the Year in 2017. When not practicing, Ms. Griffith is an avid sailor, marathoner, and long-distance cyclist.*

A Case Report of Acute Hemorrhagic Edema of Infancy with Internal Organ Involvement

By Tess MacQueen, MS, PA-C

ABSTRACT

Acute hemorrhagic edema of infancy (AHEI) is a rare, small vessel vasculitis affecting children under the age of two years old. The clinical picture begins with the rapid onset of peripheral edema and purpuric lesions on the trunk and extremities, followed by complete spontaneous recovery. Children seldom have internal organ involvement, but when they do, the course may resemble that of Henoch-Schönlein Purpura (HSP). **Case Presentation:** Here, the author describes the case of an 11-month-old boy who developed AHEI after an upper respiratory illness and a course of amoxicillin. **Conclusion:** AHEI is a benign condition despite the impressive cutaneous appearance. Internal organ involvement similar to HSP has been described and the discussion continues as to whether AHEI is a clinical variant of HSP or its own separate entity.

KEYWORDS

Acute hemorrhagic edema of infancy (AHEI), Vasculitis, Purpura, Henoch-Schönlein Purpura (HSP)

INTRODUCTION

Acute hemorrhagic edema of infancy (AHEI), otherwise known as Finkelstein disease, is a small vessel vasculitis seen in infants 4 months to 2 years of age. The cause is unknown but is believed to be an immune-mediated process associated with immunoglobulin A (IgA) deposition.[1] Many possible triggers have been reported, but the exact cause remains unclear.[2] (*See Table 1.)*

AHEI is usually preceded by a prodromal illness such as an upper respiratory illness. Cutaneous symptoms are striking but the child remains in good health and generally has an excellent prognosis. The most common presenting symptom is a diffuse rash. Characteristics of the rash include a rapid progression of target-like, or cockade wheals that persist (unlike urticaria where they typically come and go). The lesions evolve into ecchymosis and purpura over 24 to 48 hours.[4] The mucous membranes are typically not involved. Perilesional swelling is common as is swelling of the extremities. Fever may or may not be present. Involvement of the kidney and gastrointestinal tract are rare, though when they occur may present as nephritis, vomiting, transient paralytic ileus, gastrointestinal hemorrhage, bowel ischemia, intussusception, and bowel perforation.[5] When skin biopsies are performed they tend to show a leukocytoclastic vasculitis with histopathologic findings identical to Henoch-Schönlein Purpura (HSP), however the pattern of antibody staining on direct immunofluorescence (DIF) is different.[6] The differential diagnosis consists of Sweet syndrome, meningococcemia, erythema multiform, Kawasaki disease, and trauma-induced purpura.[7] These disorders can be differentiated from AHEI by history, physical examination, and laboratory studies, including skin biopsy when appropriate.

Table 1-Possible triggers of acute hemorrhagic edema of infancy

Infections	Viral upper respiratory infection Staphylococcal and Streptococcal infections Pulmonary tuberculosis Urinary tract infections Pneumonia Cytomegalovirus
Immunizations	Measles, mumps, and rubella (MMR) vaccine[3]
Medications	Penicillin Cephalosporins Trimethoprim-sulfamethoxazole

In the absence of internal organ involvement and abnormal vital signs, treatment is largely supportive and consists of hydration and identifying the causative agent. Systemic corticosteroids and antihistamines have been used but not reliably shown to be effective.[8]

CASE PRESESNTATION

An 11-month-old boy presented to the emergency department with diffuse palpable purpura, fever, colicky abdominal pain, vomiting, and irritability. He had been prescribed amoxicillin seven days prior for acute otitis media. His parents noted that a "red rash" started on his abdomen two days beforehand and spread to his extremities on the seventh day of amoxicillin treatment. They stopped giving him the antibiotic once the rash appeared. They had subsequently been giving the child

diphenhydramine and ranitidine for 24 hours. The child was up to date on immunizations, had no sick contacts, and had been otherwise well up until a week prior. Vital signs were as follows: temperature: 98.3 degrees F; pulse rate: 116 beats per minute; respiration: 30 breaths per minute; weight: 21.16 lbs (9.6 kg)

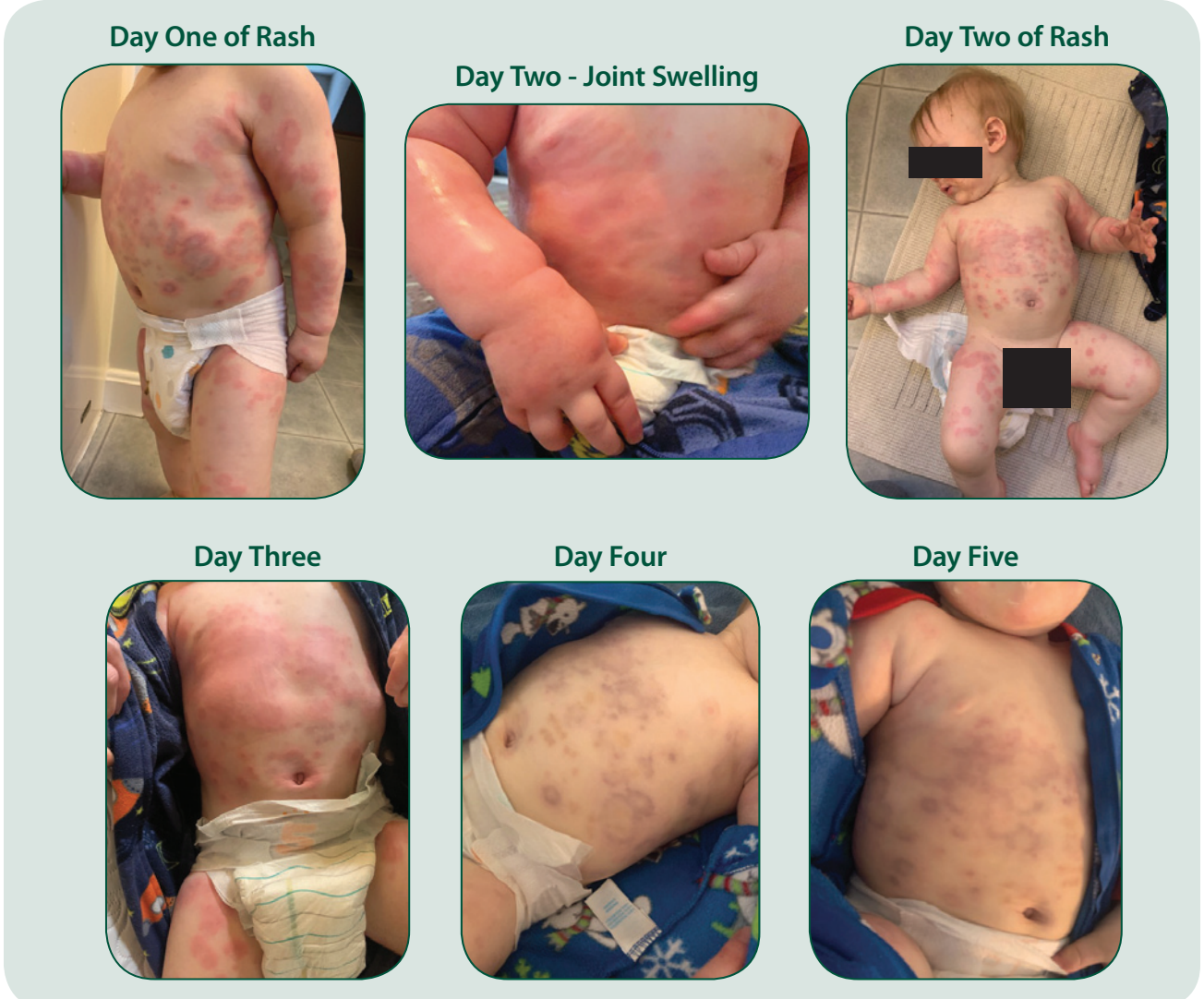
On examination, the child was alert and tearful. He had palpable purpura on his face, trunk, and extremities. His right wrist and left ankle were swollen. He had a swollen scrotum. His abdomen was soft, but he winced when palpated. He also had bouts of abdominal guarding and inconsolability. He did not have mucositis. His neurologic, respiratory, and cardiac examinations were unremarkable.

The urinalysis showed 1+ blood and fecal occult blood was positive. The complete blood count (CBC) and comprehensive metabolic panel (CMP) were normal. The c-reactive protein (CRP) was minimally elevated at 8.52 mg/L (<8.0 mg/L). An abdominal ultrasound was negative for intussusception and showed no other pathology. An abdominal x-ray showed a moderate amount of stool in the colon but was otherwise normal. A skin biopsy was not performed.

He was given a bolus of normal saline intravenously and discharged home in stable condition. On the day of discharge, he was prescribed prednisolone 15 mg/15 mL, 3.75 mL per os (PO [by mouth]) for five days. His rash resolved by day five, and subsequent urine and stool studies performed three weeks after the event were normal. A COVID-19 immunoglobulin G (IgG) serum antibody test performed four weeks later was negative. Given the child's age of less than two years, recent viral infection, antibiotic use, and distribution of symmetric edema and purpura involving the face, AHEI with internal organ involvement was favored over HSP.

DISCUSSION

AHEI has been described as a clinical variant of Henoch-Schönlein purpura (HSP). Typically, HSP is seen in children aged 3 to 15 years, whereas AHEI is seen between the ages of 4 months and 2 years. Patients with AHEI rarely have internal organ involvement, but when they do, it can present similarly to HSP.[9] The distribution of purpura in AHEI typically occurs on



the face, ears, and extremities, whereas purpura in HSP commonly spares the face and presents on the buttocks and extensor legs. Our patient illustrates the overlap between the two conditions as he presented with the classic cutaneous findings of AHEI along with findings typically seen in HSP such as arthritis, scrotal edema, and internal organ involvement as demonstrated by microscopic hematuria and hematochezia.

CONCLUSION

AHEI of infancy usually has an excellent prognosis despite its dramatic physical appearance. There is overlap between AHEI and HSP. Therefore, care must be taken to exclude internal organ involvement when AHEI is suspected. A workup should be performed when symptoms similar to HSP are present and to exclude life threatening causes of purpura.

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Tess MacQueen, MS, PA-C, is from Pine Point Medical in Lansing, New York.

***Address for correspondence**: TessMacQueen@gmail.com*

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†NBRx share as prescribed by rheumatologists, allocated using Symphony Health patient longitudinal data to limit product use to *ICD-10* codes for PsA and/or PsO. NBRx is the IQVIA NPA New to Brand® measure showing the volume of prescriptions associated with first-time patient use of a product.[2]

ACR=American College of Rheumatology; *ICD-10=International Classification of Diseases,* Tenth Revision; IGA=Investigator's Global Assessment modified 2011; PASI=Psoriasis Area Severity Index; PsA=psoriatic arthritis; PsO=plaque psoriasis.

INDICATIONS

COSENTYX® (secukinumab) is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. COSENTYX is indicated for the treatment of adult patients with active psoriatic arthritis. COSENTYX is indicated for the treatment of adult patients with active ankylosing spondylitis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

COSENTYX is contraindicated in patients with a previous serious hypersensitivity reaction to secukinumab or to any of the excipients.

Please see additional Important Safety Information on reverse. Please see Brief Summary of full Prescribing Information on the following pages.

Cosentyx® (secukinumab)

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS

Infections

COSENTYX may increase the risk of infections. In clinical trials, a higher rate of infections was observed in subjects treated with COSENTYX compared to placebo-treated subjects. In placebo-controlled clinical trials in patients with moderate to severe plaque psoriasis, higher rates of common infections such as nasopharyngitis (11.4% versus 8.6%), upper respiratory tract infection (2.5% versus 0.7%), and mucocutaneous infections with candida (1.2% versus 0.3%) were observed with COSENTYX compared with placebo. A similar increase in risk of infection was seen in placebo-controlled trials in patients with psoriatic arthritis and ankylosing spondylitis. The incidence of some types of infections appeared to be dose-dependent in clinical studies.

Exercise caution when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection.

Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and COSENTYX should be discontinued until the infection resolves.

Pre-treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COSENTYX. Do not administer COSENTYX to patients with active TB infection. Initiate treatment of latent TB prior to administering COSENTYX. Consider anti-TB therapy prior to initiation of COSENTYX in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving COSENTYX should be monitored closely for signs and symptoms of active TB during and after treatment.

Inflammatory Bowel Disease

Caution should be used when prescribing COSENTYX to patients with inflammatory bowel disease. Exacerbations, in some cases serious, occurred in patients treated with COSENTYX during clinical trials in plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. In addition, new onset inflammatory bowel disease cases occurred in clinical trials with COSENTYX. In an exploratory study in 59 patients with active Crohn's disease, there were trends toward greater disease activity and increased adverse events in the secukinumab group as compared to the placebo group. Patients who are treated with COSENTYX should be monitored for signs and symptoms of inflammatory bowel disease.

Hypersensitivity Reactions

Anaphylaxis and cases of urticaria occurred in patients treated with COSENTYX in clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of COSENTYX should be discontinued immediately and appropriate therapy initiated.

The removable cap of the COSENTYX Sensoready® pen and the COSENTYX prefilled syringe contains natural rubber latex which may cause an allergic reaction in latex-sensitive individuals. The safe use of the COSENTYX Sensoready pen or prefilled syringe in latex-sensitive individuals has not been studied.

Vaccinations

Prior to initiating therapy with COSENTYX, consider completion of all age appropriate immunizations according to current immunization guidelines. Patients treated with COSENTYX should not receive live vaccines.

Non-live vaccinations received during a course of COSENTYX may not elicit an immune response sufficient to prevent disease.

MOST COMMON ADVERSE REACTIONS

Most common adverse reactions (>1%) are nasopharyngitis, diarrhea, and upper respiratory tract infection.

References: 1. COSENTYX [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; June 2020. **2.** IQVIA NPA Weekly Tracker as of December 2019. Data on File for step-by-step PsA share calculation by Novartis Pharmaceuticals Corp.

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Cosentyx® (secukinumab)

NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

Printed in USA 9/20 COS-1394433

COSENTYX® (secukinumab) injection, for subcutaneous use
COSENTYX® (secukinumab) for injection, for subcutaneous use
Initial U.S. Approval: 2015
BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE

1.1 Plaque Psoriasis

COSENTYX® is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

1.2 Psoriatic Arthritis

COSENTYX is indicated for the treatment of adult patients with active psoriatic arthritis.

1.3 Ankylosing Spondylitis

COSENTYX is indicated for the treatment of adult patients with active ankylosing spondylitis.

1.4 Non-radiographic Axial Spondyloarthritis

COSENTYX is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.

4 CONTRAINDICATIONS

COSENTYX is contraindicated in patients with a previous serious hypersensitivity reaction to secukinumab or to any of the excipients *[see Warnings and Precautions (5.4)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Infections

COSENTYX may increase the risk of infections. In clinical trials, a higher rate of infections was observed in COSENTYX treated subjects compared to placebo-treated subjects. In placebo-controlled clinical trials in patients with moderate to severe plaque psoriasis, higher rates of common infections, such as nasopharyngitis (11.4% versus 8.6%), upper respiratory tract infection (2.5% versus 0.7%) and mucocutaneous infections with candida (1.2% versus 0.3%) were observed with COSENTYX compared with placebo. A similar increase in risk of infection was seen in placebo-controlled trials in patients with psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis *[see Adverse Reactions (6.1)]*. The incidence of some types of infections appeared to be dose-dependent in clinical studies *[see Adverse Reactions (6.1)]*.

Exercise caution when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection.

Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and COSENTYX should be discontinued until the infection resolves.

5.2 Pre-treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COSENTYX. Do not administer COSENTYX to patients with active TB infection. Initiate treatment of latent TB prior to administering COSENTYX. Consider anti-TB therapy prior to initiation of COSENTYX in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving COSENTYX should be monitored closely for signs and symptoms of active TB during and after treatment.

5.3 Inflammatory Bowel Disease

Caution should be used when prescribing COSENTYX to patients with inflammatory bowel disease. Exacerbations, in some cases serious, occurred in COSENTYX treated patients during clinical trials in plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis. In addition, new onset inflammatory bowel disease cases occurred in clinical trials with COSENTYX. In an exploratory study in 59 patients with active Crohn's disease, there were trends toward greater disease activity and increased adverse events in the secukinumab group as compared to the placebo group. Patients who are treated with COSENTYX should be monitored for signs and symptoms of inflammatory bowel disease *[see Adverse Reactions (6.1)]*.

5.4 Hypersensitivity Reactions

Anaphylaxis and cases of urticaria occurred in COSENTYX treated patients in clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of COSENTYX should be discontinued immediately and appropriate therapy initiated *[see Adverse Reactions (6.1)]*.

5.5 Risk of Hypersensitivity in Latex-Sensitive Individuals

The removable cap of the COSENTYX Sensoready pen and the COSENTYX prefilled syringe contains natural rubber latex, which may cause an allergic reaction in latex-sensitive individuals. The safe use of COSENTYX Sensoready pen or prefilled syringe in latex-sensitive individuals has not been studied.

5.6 Vaccinations

Prior to initiating therapy with COSENTYX, consider completion of all age appropriate immunizations according to current immunization guidelines. Patients treated with COSENTYX should not receive live vaccines.

Non-live vaccinations received during a course of COSENTYX may not elicit an immune response sufficient to prevent disease.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in the labeling:

- Infections *[see Warnings and Precautions (5.1)]*
- Inflammatory Bowel Disease *[see Warnings and Precautions (5.3)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Plaque Psoriasis

A total of 3430 plaque psoriasis subjects were treated with COSENTYX in controlled and uncontrolled clinical trials. Of these, 1641 subjects were exposed for at least 1 year.

Four placebo-controlled Phase 3 trials in plaque psoriasis subjects were pooled to evaluate the safety of COSENTYX in comparison to placebo up to 12 weeks after treatment initiation, in Trials 1, 2, 3, and 4. In total, 2077 subjects were evaluated (691 to COSENTYX 300 mg group, 692 to COSENTYX 150 mg group, and 694 to placebo group) *[see Clinical Studies (14) in the full prescribing information]*.

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the COSENTYX groups than the placebo group during the 12-week placebo-controlled period of the placebo-controlled trials.

Table 1: Adverse Reactions Reported by Greater Than 1% of Subjects with Plaque Psoriasis Through Week 12 in Trials 1, 2, 3, and 4

Adverse Reactions	COSENTYX		Placebo (N = 694) n (%)
	300 mg (N = 691) n (%)	150 mg (N = 692) n (%)	
Nasopharyngitis	79 (11.4)	85 (12.3)	60 (8.6)
Diarrhea	28 (4.1)	18 (2.6)	10 (1.4)
Upper respiratory tract infection	17 (2.5)	22 (3.2)	5 (0.7)
Rhinitis	10 (1.4)	10 (1.4)	5 (0.7)
Oral herpes	9 (1.3)	1 (0.1)	2 (0.3)
Pharyngitis	8 (1.2)	7 (1.0)	0 (0)
Urticaria	4 (0.6)	8 (1.2)	1 (0.1)
Rhinorrhea	8 (1.2)	2 (0.3)	1 (0.1)

Adverse reactions that occurred at rates less than 1% in the placebo-controlled period of Trials 1, 2, 3, and 4 through Week 12 included: sinusitis, tinea pedis, conjunctivitis, tonsillitis, oral candidiasis, impetigo, otitis media, otitis externa, inflammatory bowel disease, increased liver transaminases, and neutropenia.

Infections

In the placebo-controlled period of the clinical trials in plaque psoriasis (a total of 1382 subjects treated with COSENTYX and 694 subjects treated with placebo up to 12 weeks), infections were reported in 28.7% of subjects treated with COSENTYX compared with 18.9% of subjects treated with placebo. Serious infections occurred in 0.14% of patients treated with COSENTYX and in 0.3% of patients treated with placebo *[see Warnings and Precautions (5.1)]*.

Over the entire treatment period (a total of 3430 plaque psoriasis subjects treated with COSENTYX for up to 52 weeks for the majority of subjects), infections were reported in 47.5% of subjects treated with COSENTYX (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of subjects treated with COSENTYX (0.015 per patient-year of follow-up).

Phase 3 data showed an increasing trend for some types of infection with increasing serum concentration of secukinumab. Candida infections, herpes viral infections, staphylococcal skin infections, and infections requiring treatment increased as serum concentration of secukinumab increased.

Neutropenia was observed in clinical trials. Most cases of secukinumab-associated neutropenia were transient and reversible. No serious infections were associated with cases of neutropenia.

Inflammatory Bowel Disease

Cases of inflammatory bowel disease, in some cases serious, were observed in clinical trials with COSENTYX. In the plaque psoriasis program, with 3430 patients exposed to COSENTYX over the entire treatment period for up to 52 weeks (2725 patient-years), there were 3 cases (0.11 per 100 patient-years) of exacerbation of Crohn's disease, 2 cases (0.08 per 100 patient-years) of exacerbation of ulcerative colitis, and 2 cases (0.08 per 100 patient-years) of new onset ulcerative colitis. There were no cases in placebo patients (N = 793; 176 patient-years) during the 12 week placebo-controlled period.

One case of exacerbation of Crohn's disease was reported from long-term non-controlled portions of ongoing clinical trials in plaque psoriasis *[see Warnings and Precautions (5.3)]*.

Hypersensitivity Reactions

Anaphylaxis and cases of urticaria occurred in COSENTYX treated patients in clinical trials *[see Warnings and Precautions (5.4)]*.

Psoriatic Arthritis

COSENTYX was studied in two placebo-controlled psoriatic arthritis trials with 1003 patients (703 patients on COSENTYX and 300 patients on placebo). Of the 703 patients who received COSENTYX, 299 patients received a subcutaneous loading dose of COSENTYX (PsA1) and 404 patients received an intravenous loading dose of secukinumab (PsA2) followed by COSENTYX administered by subcutaneous injection every four weeks. During the 16-week placebo-controlled period

of the trials in patients with psoriatic arthritis, the overall proportion of patients with adverse events was similar in the secukinumab and placebo-treatment groups (59% and 58%, respectively). The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo groups during the 16-week placebo-controlled period were nasopharyngitis, upper respiratory tract infection, headache, nausea, and hypercholesterolemia. The safety profile observed in patients with psoriatic arthritis treated with COSENTYX is consistent with the safety profile in psoriasis.

Similar to the clinical trials in patients with psoriasis, there was an increased proportion of patients with infections in the COSENTYX groups (29%) compared to placebo group (26%) *[see Warnings and Precautions (5.1)]*.

There were cases of Crohn's disease and ulcerative colitis that include patients who experienced either exacerbations or the development of new disease. There were three cases of inflammatory bowel disease, of which two patients received secukinumab and one received placebo *[see Warnings and Precautions (5.3)]*.

Ankylosing Spondylitis

COSENTYX was studied in two placebo-controlled ankylosing spondylitis trials with 590 patients (394 patients on COSENTYX and 196 patients on placebo). Of the 394 patients who received COSENTYX, 145 patients received a subcutaneous load of COSENTYX (study AS1), and 249 received an intravenous loading dose of secukinumab (study AS2) followed by COSENTYX administered by subcutaneous injection every four weeks. During the 16-week placebo-controlled period of the trials in patients with ankylosing spondylitis, the overall proportion of patients with adverse events was higher in the secukinumab groups than the placebo-treatment groups (66% and 59%, respectively). The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo groups during the 16-week placebo-controlled period were nasopharyngitis, nausea, and upper respiratory tract infection. The safety profile observed in patients with ankylosing spondylitis treated with COSENTYX is consistent with the safety profile in psoriasis. In a third controlled study of AS (study AS3), the safety profile of the 300 mg dose of COSENTYX was consistent with the safety profile of the 150 mg dose of COSENTYX.

Similar to clinical trials in patients with psoriasis, there was an increased proportion of patients with infections in the COSENTYX groups (31%) compared to the placebo group (18%) *[see Warnings and Precautions (5.1)]*.

In the original ankylosing spondylitis program, with 571 patients exposed to COSENTYX there were 8 cases of inflammatory bowel disease during the entire treatment period [5 Crohn's (0.7 per 100 patient-years) and 3 ulcerative colitis (0.4 per 100 patient-years)]. During the placebo-controlled 16-week period, there were 2 Crohn's disease exacerbations and 1 new onset ulcerative colitis case that was a serious adverse event in patients treated with COSENTYX compared to none of the patients treated with placebo. During the remainder of the study when all patients received COSENTYX, 1 patient developed Crohn's disease, 2 patients had Crohn's exacerbations, 1 patient developed ulcerative colitis, and 1 patient had an ulcerative colitis exacerbation *[see Warnings and Precautions (5.3)]*.

Non-radiographic Axial Spondyloarthritis

COSENTYX was studied in one randomized, double-blind, placebo-controlled non-radiographic axial spondyloarthritis trial with 555 patients (185 patients on with load COSENTYX, 184 patients on without load COSENTYX and 186 patients on placebo). The safety profile for patients with nr-axSpA treated with COSENTYX was overall similar to the safety profile seen in patients with AS and other previous experience with COSENTYX. Patients in nr-axSpA1 study who received the loading dosing regimen compared to those without the loading regimen, had higher incidence of infections and infestations (92 per 100 patient-years vs 72 per 100 patient years), including nasopharyngitis, upper respiratory tract infection and urinary tract infection, and gastrointestinal disorders (27 per 100 patient-years vs 22 per 100 patient-years), including gastritis, lower abdominal pain, colitis, diarrhea, and hematochezia.

6.2 Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. The immunogenicity of COSENTYX was evaluated using an electrochemiluminescence-based bridging immunoassay. Less than 1% of subjects treated with COSENTYX developed antibodies to secukinumab in up to 52 weeks of treatment. However, this assay has limitations in detecting anti-secukinumab antibodies in the presence of secukinumab; therefore, the incidence of antibody development might not have been reliably determined. Of the subjects who developed antidrug antibodies, approximately one-half had antibodies that were classified as neutralizing. Neutralizing antibodies were not associated with loss of efficacy.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to COSENTYX with the incidences of antibodies to other products may be misleading.

7 DRUG INTERACTIONS

7.1 Live Vaccines

Patients treated with COSENTYX may not receive live vaccinations *[see Warnings and Precautions (5.6)]*.

7.2 Non-Live Vaccines

Patients treated with COSENTYX may receive non-live vaccinations. Healthy individuals who received a single 150 mg dose of COSENTYX 2 weeks prior to vaccination with a non-U.S. approved group C meningococcal polysaccharide conjugate vaccine and a non-U.S. approved inactivated seasonal influenza vaccine had similar antibody responses compared to individuals who did not receive COSENTYX prior to vaccination. The clinical effectiveness of meningococcal and influenza vaccines has not been assessed in patients undergoing treatment with COSENTYX *[see Warnings and Precautions (5.6)]*.

7.3 CYP450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Results from a drug-drug interaction study in subjects with moderate to severe psoriasis showed no clinically relevant interaction for drugs metabolized by CYP3A4.

Upon initiation or discontinuation of COSENTYX in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for therapeutic effect or drug concentration and consider dosage adjustment as needed *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Limited available human data with COSENTYX use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes. In an embryo-fetal development study, no adverse developmental effects were observed in infants born to pregnant monkeys after subcutaneous administration of secukinumab during organogenesis at doses up to 30 times the maximum recommended human dose (MRHD) *(see Data)*.

The background risk of major birth defects and miscarriage for the indicated population is unknown; however, the background risk in the U.S. general population of major birth defects is 2%-4% and of miscarriage is 15%-20% of clinically recognized pregnancies.

Data

Animal Data

An embryo-fetal development study was performed in cynomolgus monkeys with secukinumab. No malformations or embryo-fetal toxicity were observed in fetuses from pregnant monkeys that were administered secukinumab weekly by the subcutaneous route during the period of organogenesis at doses up to 30 times the MRHD (on a mg/kg basis at a maternal dose of 150 mg/kg).

A pre- and post-natal development toxicity study was performed in mice with a murine analog of secukinumab. No treatment related effects on functional, morphological or immunological development were observed in fetuses from pregnant mice that were administered the murine analog of secukinumab on gestation days 6, 11, and 17 and on postpartum days 4, 10, and 16 at doses up to 150 mg/kg/dose.

8.2 Lactation

Risk Summary

It is not known whether secukinumab is excreted in human milk or absorbed systemically after ingestion. There are no data on the effects of COSENTYX on the breastfed child or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COSENTYX and any potential adverse effects on the breastfed child from COSENTYX or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness of COSENTYX in pediatric patients have not been evaluated.

8.5 Geriatric Use

Of the 3430 plaque psoriasis subjects exposed to COSENTYX in clinical trials, a total of 230 were 65 years or older, and 32 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 years and older was not sufficient to determine whether they responded differently from younger subjects.

10 OVERDOSAGE

Doses up to 30 mg/kg intravenously have been administered in clinical trials without dose-limiting toxicity. In the event of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

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Original Research

Exploratory Study of the Association Between Spironolactone Use for the Treatment of Acne Vulgaris and Premenstrual Syndrome Symptom Improvement in Female Patients

By Megan Dauscher, MS, PA-C; Taylor Bach, MS, PA-C; Rachel Dorrer, MS, PA-C; Nicole DeMott, MS, PA-C; Christina M. Ventura, DrPH

ABSTRACT

Introduction: Premenstrual syndrome, commonly experienced by women of reproductive age, reduces the quality of life of those who experience it severely. Research on options for women who may not want to be on hormonal contraceptives to treat premenstrual syndrome symptoms are limited, although spironolactone, a potassium-sparing diuretic and selective aldosterone blocker used off-label in dermatology for treatment of acne and hirsutism in women, presents a viable choice for women with hormonal acne. **Methods:** A quantitative survey was disseminated to patients currently being treated with spironolactone at a dermatology practice in Long Island, New York, via anonymous QR codes during patient encounters. Questions captured details related to spironolactone treatment as well as demographics, premenstrual syndrome symptoms experienced before and during treatment, and self-reported quality of life and self-esteem measures. **Results:** A total of N=56 female participants responded to the survey; participant average age was 30.6 years old. While patients reported an overwhelmingly positive experience of being on the medication, as well as an improvement in their self-confidence and self-esteem being on spironolactone therapy, there was not a statistically significant association between improvement of premenstrual syndrome symptoms based on dosage and duration of therapy (p=0.726 and p=0.557, respectively). **Conclusions:** Although spironolactone has been shown in some studies to improve premenstrual syndrome symptomatology, it was not associated with an improvement in this study. Improved patient communication and interprofessional collaboration between dermatologists and gynecologists may help to better educate patients and improve their understanding of their comprehensive symptomology and subsequent symptom resolution.

KEY WORDS

Spironolactone, female hormonal acne, acne vulgaris, premenstrual syndrome, PMS, oral contraceptives, OCP

INTRODUCTION

Several studies have examined the efficacy of spironolactone in the treatment of hormonal acne vulgaris. Acne vulgaris is a chronic inflammatory skin condition, mostly affecting adolescent females. However, adult females represent a significant and increasing number of cases. According to the National Institute of Health (NIH), about 80 percent of people between the ages of 11 and 30 have outbreaks of the skin disorder at some point.[1] Acne can cause scarring, disfigurement, as well as psychological distress.[2]

Two hormonal therapies commonly prescribed for treating acne vulgaris in adult women are spironolactone and oral contraceptive pills (OCPs). Spironolactone for the treatment of acne will be touched on in much greater depth later in this article. There are three combination OCPs comprising progestin and estrogen that have been approved by the United States Food and Drug Administration (FDA) for the treatment of female hormonal acne. These are ethinyl estradiol/norgestimate, drospirenone/ethinyl estradiol, and ethinyl estradiol/norethindrone acetate/ferrous fumarate.[3,4] The most common reported side effects of OCPs include weight gain, breast tenderness, nausea, and increased risk for deep vein thrombosis (DVT).[4] However, the use of oral contraceptives has been found to be protective against the development of the two most common gynecological cancers—endometrial and ovarian.[4]

According to the American Academy of Dermatology Association, women tend to get adult acne more than men do.[5] Women often experience fluctuating hormones after discontinuing or starting OCPs or during menses, pregnancy, perimenopause, and menopause. A medical officer at the FDA's Center for Drug Evaluation and Research (CDER), Jane Liedtka, states, "There are many misconceptions out there about how acne forms, as well as on how to treat the condition." She further clarifies that there is no known way to prevent the development of acne. It is not solely caused by poor hygiene or diet and does not need to be allowed to run its course. Rather, she states that the leading causes of acne, include increase in sex hormones, hormonal changes, and genetics.[1]

One study defines the hormonal pattern of acne vulgaris by a predominance of inflammatory papules concentrated along the lower half of the cheeks, jawline, chin, and lateral neck. It is common for many of the inflammatory papules to be deep and palpable, and sometimes with nodules present. Tenderness of lesions is a common complaint, with a low number or absence of comedones.[6] However, many patients have no signs of peripheral hyperandrogenism other than acne, and serum androgens and gonadotropins are often normal.[7] Research has demonstrated the success of spironolactone in treating severe forms of hormonal acne vulgaris, including in patients whose acne had been refractory to the use of combined oral contraceptive therapy.[4]

In addition, there are other factors relating to acne, including age, smoking, and ethnicity, and endocrine and gynecological abnormalities, most commonly polycystic ovarian syndrome (PCOS).[7] Researchers have found a correlation between stress and acne flare ups. As a result of stress, the human body creates more androgens that stimulate sebaceous glands and hair follicles, which leads to acne.

Spironolactone is mainly a mineralocorticoid receptor antagonist; however, it also acts as an androgen receptor antagonist. Research has shown that spironolactone reduces androgen mediated sebum production, which is linked in the pathophysiology of some forms of acne vulgaris.[2] Spironolactone has moderate affinity for both progesterone and androgen receptors.[7] The antiandrogenic effects of spironolactone were first discovered when it was being used to treat hypertension in women with concurrent PCOS and hirsutism.[6] Spironolactone may also have a benefit over OCPs in regard to incidence of thrombosis. Research demonstrates that there is a decreased likelihood of DVT with the use of spironolactone compared to OCP therapy.[4]

Studies show that women with hormonal pattern acne with normal androgen levels have increased levels of tissue-derived androgens, 3-alpha-androstanediol glucuronide, and androsterone glucuronide. These tissue-derived androgens act locally on target tissues causing acne in females. Additionally, acne-prone skin has greater activity of type-1 5-alpha-reductase activity. Spironolactone decreases 5-alpha reductase activity via increased clearance of testosterone secondary to augmented liver hydroxylase activity. Spironolactone also increases the level of steroid hormone binding globulin which binds to testosterone, hence reducing free circulating testosterone.[6] Since spironolactone competes with dihydrotestosterone (DHT) at androgen binding receptors, it reduces overall DHT and testosterone binding. This ability of spironolactone to inhibit androgens led to its use in women with androgenic alopecia, hirsutism, and excess sebum production.[6]

ACNE, SPIRONOLACTONE, AND PMS

Premenstrual syndrome (PMS) is known to occur during the initiation of the luteal phase of the menstrual cycle.[8] Most women of reproductive age have some physical discomfort or dysphoria symptoms in the weeks prior to menstruation. PMS symptoms can range in severity, from mild to severe enough to affect one's daily functioning and activities.[9] Some PMS symptoms include irritability, bloating, depression, feeling of swelling, breast tenderness, and food cravings. Some studies suggest that up to 20 percent of women of reproductive age experience some form of premenstrual complaints; however, it is estimated that 5 to 8 percent of women suffer from moderate-to-severe PMS symptoms. Additionally, it is estimated that the lifetime comorbidity between PMS and other mood disorders range from 30 to 70 percent. Also, anxiety and panic disorders occur at a higher rate in women who experience PMS.[9] The length of PMS symptom expression ranges from days to up to two weeks. The most severe symptoms tend to occur within six days prior to menses, peaking about two days prior.[9]

Mood changes in PMS are due to probable causative factors, including an abnormal neurotransmitter response during the luteal phase of menstruation. PMS symptoms then diminish when estradiol and progesterone dominate during the follicular phase. Similar to benzodiazepines, progesterone has an anxiolytic effect and agonizes gamma-aminobutyric acid (GABA) receptors in the central nervous system. On the contrary, steroid androgens are an "inverse agonist" of the benzodiazepine site of GABA receptors inducing an abnormal response creating an anxious effect. Somatic symptoms such as breast tenderness, bloating, and muscle pains result from changes in hormone-responsive tissues in the periphery. Some studies have suggested the involvement of aldosterone in the pathophysiology of premenstrual bloating.[10]

Many treatment options are available for effective treatment of PMS, but few are supported by clinical evidence. Selective serotonin reuptake inhibitors (SSRIs) have shown a reduction in mood disturbance and somatic complaints, as well as improvement in overall functioning. Additionally, due to the role of sex hormones in triggering PMS symptoms, many treatments target these molecules. These treatments include, but are not limited to, OCPs, gonadotropin-releasing hormone (GnRH) agonists, and danazol, the androgen and gonadotropin inhibitor. Because of its diuretic properties, spironolactone may be effective in the treatment of bloating and breast pain associated with PMS due to the relationship between PMS and water retention.[9] Furthermore, spironolactone decreases circulating steroid androgens, decreasing the incidence of PMS symptoms.[8] However, there is limited evidence correlating spironolactone and treating PMS, a disorder likely correlated with the development and progression of hormonal acne vulgaris.

Research has been performed in the past that examined both the safety and efficacy of spironolactone in the treatment of acne vulgaris. However, there are limited studies on the correlation of spironolactone and the improvement of PMS related symptoms in female patients with hormonal acne vulgaris. One study suggests that the diuretic effect of spironolactone may benefit women who experience premenstrual acne flares associated with fluid retention.[7] Another study has shown that spironolactone has positive effects on improving mood changes and somatic symptoms in patients with co-associated PMS. This study found that spironolactone significantly improves mood symptom scores and daily somatic symptom self-evaluation scores and has lasting effects when compared to the placebo.[8] However, other possible explanations on the pathophysiology are still being studied today and a definitive relationship has yet to be determined. The purpose of this research study is to elucidate the correlation between the use of spironolactone in female patients with hormonal acne and the associated changes in their PMS-related symptoms.

METHODS

The target population for this study was female patients currently taking spironolactone for hormonal acne vulgaris. A digital survey designed and hosted through an online platform (Qualtrics, SAP) collected and analyzed data. The survey was distributed in multiple dermatology offices, on social media, and on dermatological and physician assistant online forums. This allowed for the analysis of patients across the United States; however, the majority of sampling comprised patients from an outpatient practice in Long Island, New York. All survey responses were anonymous, obtained through random selection, and no identifying information was requested. Participants were able to either scan a QR code using their mobile device or follow a web link that brought them to the survey. Patients were given the option to complete the survey in office while waiting to be seen by their provider.

The survey comprised 24 questions that addressed the patient's demographics, their experience with acne and spironolactone, as well as details about their menstrual cycle and premenstrual syndrome symptoms. There was no age restriction on the patients that could participate. The average age of participants was 30.63 years old (range: 17 to 54 years old) *(Figure A).* The majority of participants identified themselves as Caucasian, (77.05%), and the rest answered as follows: Hispanic (11.48%), African American (3.28%), Asian (3.28%), Middle Eastern (1.64%). A small percentage (3.28%) checked that they "preferred not to answer." *(Figure B).* There was a total of 56 participants, with all participants being women. The number of months on spironolactone ranged from 1 month to 84 months and average duration of spironolactone therapy was 18.25 months *(Figure C).* The survey included multiple reasons for the use of spironolactone in addition to acne vulgaris, such as androgenic alopecia and hidradenitis suppurativa.

The survey also asked whether patients were taking any other medications while on spironolactone, including OCPs, antidepressants, or other acne-related medications *(Figure D).* However, only the results pertaining to the use of spironolactone were specifically analyzed. The survey also considered whether the female participants had pre-existing PMS symptoms to use as a baseline for comparison after starting therapy with spironolactone. The survey asked the participants to specify which symptoms, if any, had improved *(Figure E).* Several questions were sampled from the Dermatology Quality of Life Index (DLQI), a tool designed to measure the health-related quality of life (QoL) of adult patients suffering from a skin disease, to examine patients' reported QoL before starting spironolactone and during the last week of taking the medication. Additionally, the patients were asked if they had ever been diagnosed with other endocrine or gynecological abnormalities that could influence acne and PMS symptoms, such as PCOS, endometriosis, uterine fibroids, Cushing's disease, Addison's disease, hypo- or hyperthyroidism.

To further analyze the data that was collected in the survey, statistical product and service solutions (SPSS) software was used. This enabled us to see not only improvement of acne symptoms but also quality of life and improvement of premenstrual symptoms. From the data collection, an exploratory study of the correlation between the use of spironolactone for acne vulgaris and associated improvement in PMS symptoms was successfully conducted.

The study first started by identifying dependent versus independent variables. The independent variables comprised the following: 1) the underlying reason the patient was prescribed spironolactone, 2) the daily dose prescribed, 3) adherence to medication instructions, 4) rate of improvement in acne vulgaris symptoms since beginning spironolactone, and 5) the duration of therapy. The dependent variables included the following: 1) whether the participants experienced PMS symptoms prior to starting spironolactone, 2) rate of improvement in PMS symptoms since beginning spironolactone, and 3) whether their menstrual periods were ever classified as irregular as previously diagnosed by a healthcare provider (self-report). Three specific survey questions were further analyzed utilizing Chi-square analysis: rate of improvement in acne vulgaris since starting spironolactone, rate of improvement in PMS symptoms since starting spironolactone, and regularity of patient menstrual cycles.

The results were separated into groups based on the mean duration of therapy; Group 1 represented those who were taking spironolactone for 1 to 10 months and Group 2 represented therapy duration of 11 months and longer The study also separated participants by age; Group 1 represented those 17 to 26-years old and Group 2 represented participants 27-years old and older.

The following aspects of the study were analyzed using descriptive statistics—race, diagnosis associated with prescribed spironolactone use, which PMS symptoms improved with the use of spironolactone, diagnosis of another gynecological or endocrine abnormality, and side effects experienced while taking spironolactone.

Chi-square analyses were conducted to explore statistically significant associations between aspects of spironolactone treatment regimens and symptoms of PMS. Statistical significance was determined at the α=0.05 level.

RESULTS

A total of 56 participants answered the 24-question survey. *Figure A* illustrates the age group of participants in the study. Twenty-six participants who answered this survey were 26 years of age or younger and 30 participants were 27 years of age or older. *Figure B* demonstrates the race and ethnicity prevalence of the population size that

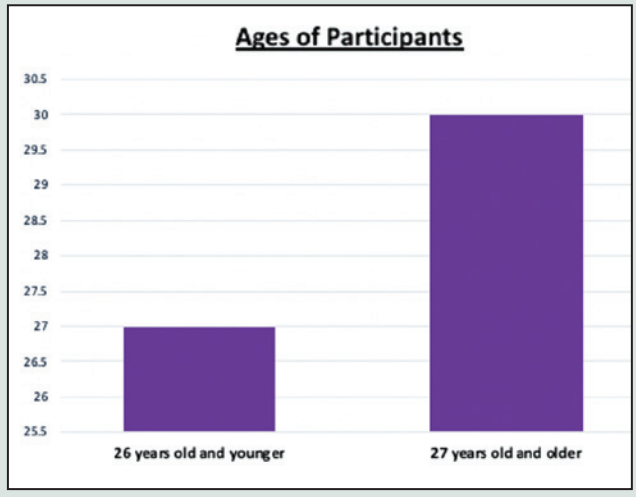

Figure A. *Patient Age Groups (divided into 26 years old and younger and 27 years old and greater). Sample taken from participants who responded to the question, "How old are you in years?"*

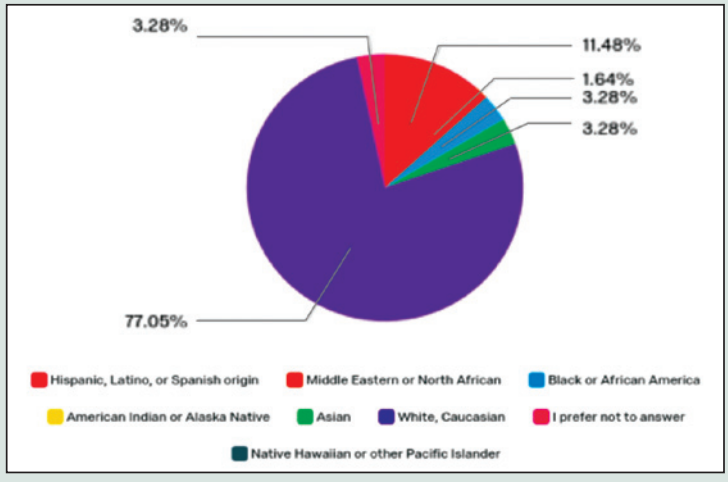

Figure B. *Patient Race and Ethnicity. Sample taken from participants who responded to the optional question "Please choose which describes you?"*

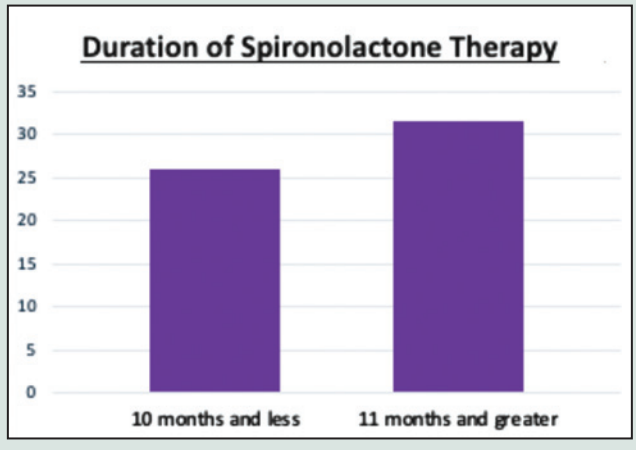

Figure C. *Duration of Therapy with Spironolactone (divided into less than or equal to 10 months or greater than or equal to 11 months). Sample taken from participants who responded to "How long have you been taking spironolactone (in months)?"*

was sampled. According to the results, 11.48 percent of participants indicated that they were of Hispanic, Latino, or Spanish origin; 77.05 percent answered that they were White or Caucasian, 3.28 percent Black or African American; 3.28 percent Asian; 1.64 percent Middle Eastern or North African; 3.28 percent checked that they preferred not to answer.

The patient reported dosages of spironolactone varied from 50 to 200 mg with the majority of the study participants taking 100 mg (55%). Thirty-one percent of patients were taking 50 mg of spironolactone while about 10 and four percent of patients reported taking 150 mg and 200 mg, respectively. *Figure C* represents the duration of spironolactone therapy. In addition, the study analyzed the underlying condition of each patient for which spironolactone was being prescribed to treat. A total of 94.6 percent of participants said that they were prescribed spironolactone to treat acne, while 1.8 percent said they were taking it for hidradenitis suppurativa (HS), 5.4 percent for androgenic alopecia, and 5.4 percent selected "other" but did not specify further.

The study also explored whether the participants had a concurrent diagnosis of an endocrine or gynecologic abnormality. According to the results, 1.8 percent had Addison's Disease, 5.4 percent had hypothyroidism or hyperthyroidism antihypertensive medications self-reported, 7.1 percent had PCOS, 3.6 percent had uterine fibroids, 3.6 percent noted having an endocrine or gynecologic condition not listed, and 73.2 percent of patients denied ever being diagnosed with an endocrine or gynecologic abnormality. Figure D displays the breakdown of participants who reported taking other prescription medications that could have impacted the results of the study. After analysis, 22.97 percent of patients stated they were not taking any other prescription medications, 27.03 percent said they were also taking OCPs, 20.27 percent stated they were also taking antidepressants or anxiolytics, 20.27 percent stated they were taking "other" prescription medication, 5.41 percent answered that they used antihypertensives medications, and 4.05 percent stated they were on "other oral acne prescriptions," such as oral antibiotics.

"Other" responses included the following: pantoprazole (Protonix), which is used to treat erosive esophagitis and other conditions involving excess stomach acid, levothyroxine (Synthroid), amphetamine-dextroamphetamine (Adderall), Vyvanse (lisdexamfetamine dimesylate), trazadone, phentermine, a hormonal intrauterine device (IUD), topiramate, pyridostigmine

Figure E illustrates whether participants noted improvement in their PMS symptoms while on

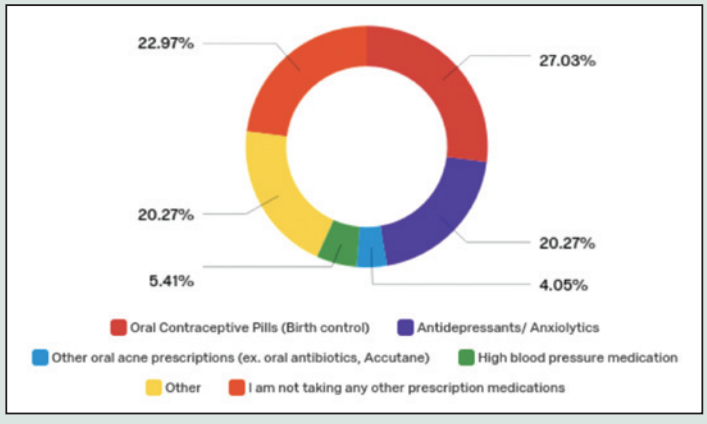

Figure D. *Concurrent Medications Taken While on Spironolactone. Sample taken from participants who responded to "Are you currently taking any other prescription medications?"*

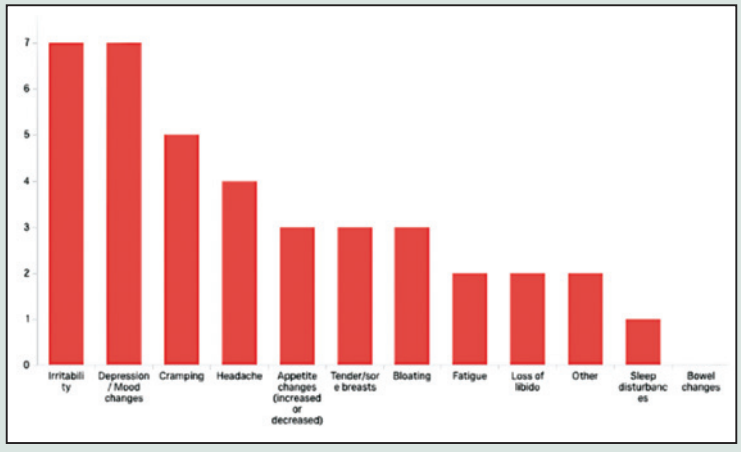

Figure E. *Symptom Improvement with Spironolactone. Sample taken from participants who responded to "If you have experienced improvement in one or more PMS symptoms, please choose which symptoms improved."*

	50-100 mg	More than 100 mg	6 months or less	More than 6 months	Regular Menses	Irregular Menses
Excellent	1 (2%)	0 (0%)	1 (2.0%)	0 (0%)	1 (2%)	0 (0%)
Good	13 (26%)	1 (2%)	4 (7.8%)	9 (17.6 %)	9 (18%)	4 (8%)
Poor	13 (26%)	2 (4%)	7 (13.7%)	10 (19.6%)	12 (24%)	4 (8%)
I did not experience PMS Symptoms Prior	16 (32%)	4 (8%)	7 (13.7%)	13 (5.9%)	13 (26%)	7 (14%)

Figure F. *Number of Patients Who Noted Improvement in Their PMS Symptoms Since Beginning Spironolactone.*

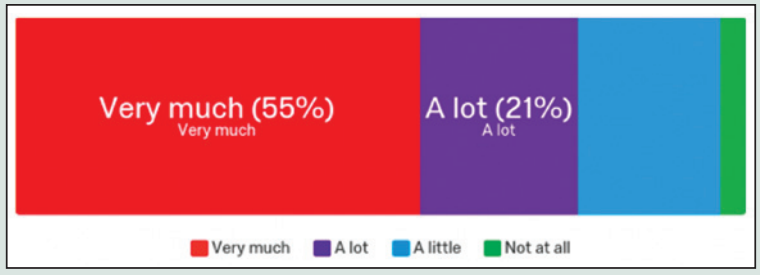

Figure G. *Quality of Life Prior to Taking Spironolactone. Sample taken from participants who responded to "Prior to starting spironolactone, how embarrassed or self conscious have you been because of your skin?"*

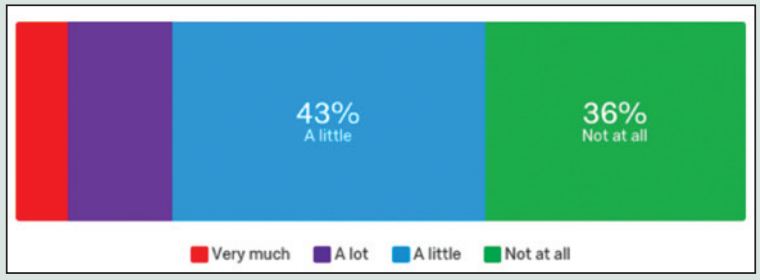

Figure H. *Quality of Life Since Beginning Spironolactone. Sample taken from participants who responded to "Within the last week, how embarrassed or self conscious have you been because of your acne?"*

spironolactone. According to the results, patients reported improvements in irritability (12.5%), depression or mood changes (12.5%), cramping (8.9%), headache (7.1%), appetite changes (5.4%), tender or sore breasts (5.4%), bloating (5.4%), changes in libido (3.6%), fatigue (3.6%), "other" changes (3.6%), and sleep disturbances (1.8%). Figure F breaks down how participants rated their PMS symptom improvement based on dosage, duration of therapy, and whether their menstrual cycles were classified as regular or irregular. According to Chi-Square analysis, Self-reported improvement of PMS symptoms was not significantly associated with spironolactone dosage, duration of therapy, and self-reported clinician diagnosis of irregular periods.

Patients were asked whether they experienced any side effects since beginning spironolactone therapy. Out of the 56 participants, 15 percent reported that they experienced dizziness and lightheadedness, 3.33 percent experienced nausea or vomiting, five percent experienced changes in urination, 13.33 percent experienced breakthrough bleeding or spotting, 8.33 percent experienced breast tenderness, and five percent stated "other" side effects. Overall, 50 percent of participants did not experience any side effects.

In order to gauge the effect of acne on a patient's daily QoL, participants were asked to rate their level of embarrassment with respect to their skin prior to taking spironolactone, and within the last week of being on the medication. According to the study, 55.36 percent of participants were "very much embarrassed" of their skin prior to starting spironolactone, 21.43 percent were "embarrassed a lot," 19.64 percent were "a little embarrassed," and 3.57 percent were "not embarrassed at all" *(Figure G)*. Within the last week of being on spironolactone, 7.14 percent of participants report that they were "very much embarrassed" of their skin, 14.29 percent were "embarrassed a lot," 42.86 percent were "a little embarrassed," and 35.71 percent were "not embarrassed at all" *(Figure H)*.

The study further explored how patients described their improvement of acne. These results were broken down based upon the dosage patients were currently taking, the duration of therapy, and whether they classified their menstrual cycles as being regular or irregular *(Figure I)*. Self-reported improvement of acne occurrence was not statistically associated with spironolactone dosage (P=0.772) or self-reported prior clinician diagnosis of irregular periods (P=0.160).

	50-100 mg	More than 100 mg	6 months or less	More than 6 months	Regular Menses	Irregular Menses
Excellent (No new breakouts)	9 (17.3%)	1 (1.9%)	4 (7.5%)	6 (1.1%)	5 (9.6%)	5 (9.6%)
Good (few new breakouts)	31 (59.6%)	6 (11.5%)	11 (20.8%)	26 (49.1%)	28 (53.8%)	9 (17.3%)
Poor (many new breakouts)	1 (1.9%)	0 (0%)	2 (3.8%)	0 (0%)	2 (3.8%)	0 (0%)
None (same as baseline)	4 (7.7%)	0 (0%)	2 (3.8%)	2 (3.8%)	1(1.9%)	2 (3.8%)

Figure I. *Number of Patients Who Noted Improvement of Acne Since beginning Spironolactone Acne improvement based on dose (n=52 [p=0.772]), improvement based on length of therapy (n=53 [p=0.203]), improvement based on regular or irregular menses (n=52 [p=0.160]).*

While not thematically coded, patients provided feedback on their spironolactone therapies that suggested an improvement in aspects of their quality of life, as per the following quotes:

> *"completely changed my skin and life. I truly feel like a new person with ten-times the confidence I used to",*
>
> *"so far so good - I am grateful for an alternative to birth control, antibiotics or Accutane",*
>
> *"it has helped clear up my horrible hormonal acne that I thought would never go away and I absolutely love using it".*

DISCUSSION AND IMPLICATIONS FOR FUTURE RESEARCH

This study analyzed the association between spironolactone use and PMS symptom improvement in female patients with hormonal acne in a dermatology setting. The majority of patients stated that they had been taking spironolactone for 11 months or longer (Figure C). The study also explored relationships between acne improvement, changes in QoL, and other gynecological issues. Many aspects of daily life are affected by chronic inflammatory skin conditions such as acne vulgaris. The study analyzed some aspects of QoL, such as patient level of embarrassment and self-consciousness with regard to their skin, effects on patient social life, and how the condition of their skin may affect their relationships with others such as close friends and relatives. The study found that the majority of patients had improvement in QoL measures. Prior to initiation of therapy, over half of the survey population (55%) patients noted that they were "very much" embarrassed and self-conscious due to their acne. After an extended course of spironolactone, almost three-quarters of the sample (69%) reported feeling "a little" or "not at all" self conscious.

A majority of participants denied ever being diagnosed with a gynecological abnormality. However, several participants stated that they had also been diagnosed with PCOS. PCOS may impact a patient's severity of PMS symptoms as well as their acne distribution and severity. Therefore, further research may be conducted between dermatology and obstetric and gynecological (OBGYN) providers, given that both specialties utilize spironolactone in treatment of hormonal conditions. Future research might also investigate the likelihood of an OBGYN provider to discuss spironolactone as a treatment option for hormonal acne and/or PMS symptoms. Similarly, future research may be performed to determine the likelihood of dermatology providers to educate their patients on the potential benefit of spironolactone for PMS symptom improvement.

In addition, the study evaluated participants on other pharmacological therapies that could impact their acne vulgaris severity, along with their PMS symptoms. About 27 percent of participants noted to be simultaneously taking OCPs with spironolactone. This can have numerous impacts. For instance, OCPs help maintain a hormonal balance which can influence and help treat acne vulgaris. Also, OCPs have been shown to be beneficial in the treatment of PMS symptoms. However, a similar percentage of participants (22.97%) stated they were not taking any other pharmacological medications. Future research could explore the efficacy of spironolactone as independent therapy versus the efficacy of spironolactone when combined with other treatment options such as OCPs. This also provides a topic of discussion for OBGYN providers and their patients who have optimized their contraceptive treatment response but are still experiencing breakthrough acne or PMS exacerbations.

In terms of spironolactone usage with the improvement of PMS-related symptoms, the majority of patients either noted that they had poor improvement of their PMS symptoms since beginning therapy or that they did not experience any PMS symptoms prior to beginning therapy. However, many patients still noted that they had "good" improvement of their PMS symptoms. The majority of patients who experienced some improvement had been taking spironolactone for six months or longer. Of those who noted improvement in PMS symptoms, the largest reported improvement was in irritability, depression, mood changes, and cramping, although these results were not found to be significant *(Figure F).*

Many past studies have confirmed the efficacy of spironolactone as a treatment for hormonal acne vulgaris.[6] Although the drug is used as an "off-label" treatment for acne, it has been widely utilized in dermatology settings

since the 1980s and has been generally well tolerated. Based on the findings from this study, the largest reported side effect was dizziness/lightheadedness, followed by breakthrough bleeding or spotting. However, half of the patients who took the survey noted that they had not experienced any side effects while taking spironolactone. Therefore, we can conclude that overall this drug is well-tolerated in the use of treatment of acne vulgaris and could be considered in clinical scenarios in which antibiotics or isotretinoin are not viable options for the patient.

Although this study displayed intriguing results, it had a number of limitations that should be considered. While there were observed improvements of patients who experienced reduced acne and improved quality of life from their acne, these associations were not statistically significant. It is important to consider, that the small sample size of this study (N=56) may have hindered the appropriate examination of meaningful statistical associations between spironolactone treatment regimens and acne resolution, QoL improvement, and PMS symptom resolution. Additionally, nearly all study participants were recruited from one outpatient setting in Long Island, New York, which may hinder generalizability of study results to medical practices in different geographic areas. Another limitation of the methods was that only dermatology platforms were utilized for recruitment. Another limitation of the study was that some results may be underestimated as some patients may have been post-menopausal when reporting severity of PMS symptoms. Additionally, some results may have been underestimated because participants were currently taking other prescription acne medications and/or OCPs. Another limitation of the study is that patient compliance with medication was not assessed. For spironolactone to be most effective, compliance is essential. If patients are noncompliant, this can limit the efficacy of the medication and, in turn, alter the patient's satisfaction with treatment. Also, the survey failed to ask if the participants changed their dosage of spironolactone in the past or during the time the study was conducted. Therefore, the study was unable to determine whether an adjustment in dosage impacts the improvement in patients' acne and PMS symptoms. Future studies should strive to recruit a larger sample size from a variety of medical practices and prescribing clinicians to facilitate statistical analysis and adjustment for potential biases in exploring the association between spironolactone and beneficial dermatological and gynecological clinical outcomes, as well as details related to treatment compliance.

CONCLUSION

This study examined the correlation between the use of spironolactone in the improvement of acne vulgaris and PMS symptoms. The study illustrated that some participants did note an improvement in their acne vulgaris and PMS symptoms with the use of spironolactone, though results failed to obtain statistical significance. Future research with a larger sample size may be able to elucidate a more definitive relationship between the aforementioned variables. Dermatology, family medicine, and OBGYN, are three specialties that can work side by side in the future to better assess this correlation. Spironolactone is a versatile medication that can affect many conditions, including acne vulgaris and PMS. The use of spironolactone as a treatment for various conditions continues to be studied and, with future research, the utility of this medication will continue to grow.

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Megan Dauscher, MS, PA-C, *is a physician assistant for the Dermatology Service at Memorial Sloan Kettering Cancer Center in Hauppauge, New York, and a guest lecturer and Master's Thesis Advisor of the Hofstra University Physician Assistant Studies Program in Hempstead, New York.*

Taylor Bach, MS, PA-C, *is a physician assistant in the Department of Medicine at North Shore University Hospital, part of Northwell Health, in Manhasset, New York.*

Rachel Dorrer, MS, PA-C, *is a physician assistant at Empire Dermatology in East Syracuse, New York.*

Christina Ventura, DrPH, *is an assistant professor of physician assistant studies at Hofstra University in Hempstead, New York.*

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Address for Correspondence: *Megan Dauscher, MS, PA-C; mdausc1@pride.hofstra.edu*

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SDPA Member Spotlight

Dermatology Physicians Assistants Strong, Essential to COVID-19 Response Coast to Coast

PART 1: EAST COAST
New York City—The "Insane Experience" of Working on Frontlines at Height of COVID-19 Pandemic

An Interview with Jang Mi Johnson, PA-C

Introduction

By Mark Hyde, PhD, PA-C

As physician assistants, we have a unique skill set that places us in a good position to adapt when necessary. While we may specialize in Dermatology, our education and training encompasses multiple aspects of general healthcare. The didactic year, in a typical PA program provides foundational medical knowledge through lectures, labs, and regular coursework. The clinical year is when PA students apply that knowledge to practice, gaining hands-on experiences in clinical settings. Students spend valuable time not only honing their patient care skills but also learning how to interact with the entire care team, an often-overlooked strength in any working environment.

Early this year when COVID-19 spread like a tidal wave around the world, we all felt its tumultuous ripple effects in our personal and professional lives. Mass closures of schools, complete shutdowns of businesses, and limited in-person health visits translated to reduced staff and, for many, furloughs or layoffs. We watched as our beloved cities—Seattle on the west coast and New York City on the east—once bustling with life, became epicenters of the country's largest health crisis in over a decade. The need for assistance was evident, and PAs proved to be an essential part of the response, further illustrating the flexibility of the PA profession. Here, we highlight some of our very own in dermatology PAs who experienced the coronavirus pandemic first-hand in those early epicenters.

I want to express my gratitude to all of those on the frontlines of this unprecedented health crisis and pride in our PA colleagues making a difference everywhere.

Respectfully,
Mark Hyde, PhD, PA-C

***Mark Hyde** is Editor in Chief of the Journal of Dermatology for Physician Assistants. He is Assistant Professor of Dermatology, Melanoma and Cutaneous Oncology Program at the Huntsman Cancer Institute in Salt Lake City, Utah.*

Jang Mi: I guess I could start at the beginning. In mid-March 2020, when the COVID-19 situation was getting really serious around the country, the dermatology company where I worked for the past 12 years informed employees that they were enacting temporary layoffs. It was the first time in my life I didn't have a job or work, and I really didn't know what to do. Then, New York Governor Andrew Cuomo wrote an executive order that allowed you to work in the state without the New York state license as long as you were licensed elsewhere. The need to have a collaborating physician was also eliminated.

I had a weird realization and thought, "There is a major health crisis happening right now. I have medical skills, and I'm sitting at home." So, after some consideration, I decided to come to New York through an agency that was sending people there to work.

Mark: I understand what you are saying about suddenly finding yourself sitting at home waiting to return to work. I did it for six full weeks.

Jang Mi: That's why I decided to come here. As much as I might have loved to stay home and garden, it just didn't feel right.

I was assigned to Elmhurst Hospital in Queens, New York, which became completely dedicated to COVID patient care in response to the pandemic. Everything was focused on treating patients coming in with COVID; if you didn't have COVID, we would try to get you out of the hospital as quickly as possible. When I started, I was assigned to the emergency room because I had prior experience working in emergency and surgical care.

Mark: When was that? How long has it been since you've done that?

Jang Mi: Before I went to PA school, I was a patient care tech. I did the blood draws and IVs, assisted in the ER and hands-on patient care. Then, I worked in general surgery as my first job as a PA

from 2002 to 2005. From 2005 to present, I've worked in dermatology, so I found it interesting to revert to the hospital environment.

Mark: I bet. It's a scary thing to do. I think about it, and it intimidates me.

Jang Mi: You know, I was scared but noticed that the majority of providers that came to work at Elmhurst Hospital in response to COVID also didn't necessarily get assigned to work in their current area of practice. There were a lot of new graduates working their very first job, which must have been frightening. Even with 17 years of experience in the medical setting—and I've said this a million times—I was not prepared to see what I saw working in the emergency room during the height of the COVID-19 pandemic.

I was having a discussion with my husband about COVID-19 media coverage and he said he wished there were more focus on people who were recovering from coronavirus or those without severe symptoms rather than reporting deaths. I explained to him that as a healthcare worker caring for patients with COVID, I only saw the people who were dying from the disease. I didn't see anybody who had a slight cough, no fever, and got better in a couple weeks. For me, my world was, "corona kills everybody."

Even with 17 years of experience in the medical setting—and I've said this a million times—I was not prepared to see what I saw working in the emergency room during the height of the COVID-19 pandemic.

It the ER, it was insane. The Elmhurst Hospital ER has two specific sides, a cardiac unit and a fast track area. The fast track area was set up for people who were on bilevel positive airway pressure (biPAP) and continuous positive airway pressure (CPAP) and high-flow nasal cannula (HFNC) therapy to hopefully keep them oxygenated so they didn't have to go to the next step. The cardiac unit became the intensive care unit (ICU) portion of the ER where everyone was intubated.

Mark: So those were COVID patients in the cardiac unit on ventilators because there was nowhere else for them to go?

Jang Mi: Right.

Mark: How many beds were in each of those units? What was the intended capacity and what were you guys dealing with?

Jang Mi: The fast track area typically had a 20-bed capacity, but during the height of COVID in March and April, I would say there were easily about 30 to 40 people in that room. The beds, some of which were transport stretchers, were so close together that sometimes you would have to squeeze between them to see a patient. The cardiac unit operated at their normal capacity—maybe 10 or 15 beds—mainly because the equipment took up any space that might have accommodated extra patients. The other side of the ER, the A side, was where the non-COVID emergencies were seen. I worked on the B side, which was strictly the COVID side. If you came into A side and had COVID symptoms, they sent you to the B side.

The place was so full there were patients on stretchers side by side, touching each other because we just didn't have the space. They were double stacked, so we had a row against the back wall and then right in front of them was another row with all the patients side by side by side. We had giant oxygen tanks all over the place with these tentacle-like connectors along the floor where you might have eight patients hooked up to one machine. The oxygen tanks were constantly running out, and we had to run down to the basement to get new ones. It was insane; I will just say that. When I got there, there were probably 100 patients in the emergency side, which was only meant to hold 25.

Mark: With the A side still seeing regular emergent and trauma cases, they had to keep those people separate from the infectious B side that was housing patients with COVID, right?

Jang Mi: Right. We were wearing full personal protective equipment (PPE)—the bunny suits with hoods and face shields. In the ER, we could get a new respirator mask every day, but you had to wear the same one for a whole 12-hour shift.

My experience working in the ER was just insane. People who had been in the ER and were already admitted to the hospital had to stay in the ER because the hospital was at full capacity. These patients remained in the ER until either someone was discharged or died, opening a room upstairs. It was bad. From my perspective, you could tell that some of the patients were going to be fine. You thought, "they'll make it through this. They'll be fine," and you felt good about that. But there were some people coming in who looked as though they were not going to live through the disease.

The second time I came to Elmhurst to work in COVID response, I was assigned to the medicine team, functioning mostly as a hospitalist. When I arrived the second time in June 2020, I felt grateful that I actually saw a patient who was admitted when I worked in the ER. He was still in the hospital but no longer intubated, and we eventually discharged him. He was in the hospital for almost two full months.

Mark: Was he otherwise healthy? Did he have any underlying conditions?

Jang Mi: Actually, we found out he had undiagnosed latent tuberculosis (TB). Other than that, he was healthy.

It was nice to come back and see this patient in the hospital and then see him leave. He was the first patient that I saw from start to finish that we discharged. I still don't know what happened to the other patients I saw when I started in the ER—whether they were discharged or what their course in the hospital was—because I wasn't on medical units while I was here the first time.

Mark: It sounds like the majority of patient cases you saw were pretty ominous.

Jang Mi: Yeah. Most of them were. One thing that I observed about the virus is that younger people—those who say, "Oh, I'm young and this doesn't really affect me"—the younger people were the ones dying the fastest. For instance, if they came in with low oxygen saturation, even if they didn't look like they were in poor health, when they went south, they went down fast. In contrast, surprisingly, the older patients would appear to be in bad shape but tended to kind of just chug along for quite some time. I think in the case of the older patient population, provided an individual didn't have a lot of pre-existing medical conditions or severe comorbidities from COVID-19, they had a chance of making it through as long as their bodies could weather the worst of the cytokine storm. In the younger patient population, I observed that those individuals appeared to be able to tolerate the low oxygen levels for a while until, all of a sudden, their bodies could no longer handle the deprivation.

For me, my world was, "corona kills everybody."

Mark: So, is it fair to say the younger patients may be coming in later in the course and not realizing the severity of their disease states?

Jang Mi: Right. They are asymptomatic much longer, and I think that's what really drives their faster demise. Most people I saw come into the ER in their 30s, if they had an oxygen saturation level below 85 percent, we could make an accurate guess that they were probably going to be on a CPAP or intubated within a few hours of admission. Once intubated, there's only a small percentage of people who are able to be extubated.

Mark: So, you were talking about the teams you were working with—PAs, NPs, MDs, etc. It sounds like almost everybody you worked with during both visits was transplanted from somewhere else and not native to Elmhurst Hospital.

Jang Mi: Many health care providers I worked with were transplants and not regular Elmhurst employees because a lot of those native to the New York area got sick [with COVID-19]. Many clinicians were treating patients before they knew what was happening with coronavirus, working in direct contact with infectious patients with little or no PPE. When I first arrived, most of us working in the ER were from agencies with a few established attendings. Although it was definitely an experience, I can't say that I would do it again. Let me rephrase that—I would do it again, but I wouldn't do it under the same conditions as when I worked in the ER during my first trip (i.e., working 12-hour shifts for 21 days straight). During my second trip, my schedule was less intense, working five 12-hour shifts per week (Wed through Sunday) with Monday and Tuesday off.

Mark: What differences have you observed between working in the spring versus summer of 2020 [during the COVID-19 pandemic]? How about differences in your assignments—ER side versus medical side of patient care?

Jang Mi: The second time around, June/July 2020 working in medical, I've noticed a slower pace than I experienced in March/April 2020 while in ER care. The medical team that I was on in the summer, which comprised PAs and NPs, managed more of what could be considered "normal" hospital issues, transitioning back to a more usual, pre-COVID care model. At that time, we had three units that were COVID only, and I saw the normal hospital admissions; nursing home residents with sepsis and things like that. Also, during my second trip, although COVID cases appeared to lessen, I did observe more ER visits for shortness of breath, cough, and the other well-known COVID symptoms, which made me wonder at the time whether New York's second wave was coming, which was scary but less so since we now know more about COVID.

Mark: How did you cope? I'm guessing you may have had some rough emotional times during those first 21 days and then again in June/July while working on the medical side. What kind of things have you done to stay healthy emotionally?

Jang Mi: Well, I do yoga regularly, so I kept that up while in New York and I also had FaceTime calls with my family almost every day.

Mark: For readers' context, can you tell us a little about your family?

Jang Mi: I have two boys aged 7 and 11. They stayed back home in Chicago with my husband while I worked in New York. They are very adventurous and, interestingly enough, while I was away working, all three of them got COVID-19.

Mark: So, they've all had it? Did that scare you to death?

Jang Mi: It did. Another reason I had FaceTime calls with them every day was so I could make my own health assessments. I asked my husband to provide constant updates on how they were feeling because I needed to know whether I had to come home.

Mark: What symptoms did your husband and sons experience? What was the severity of their illnesses?

Jang Mi: My husband only had the loss of sense of smell and found that by monitoring every day his oxygen saturation levels never fell below 95 percent, so he was fine. My youngest son had fever and diarrhea, but he didn't develop any skin rashes. My older son appeared to only have loss of smell. They were all tested, and all came back positive for COVID-19. I thought, "Of course…I'm the one in the thick of it, and I'm the only one [in my immediate family] who doesn't have it!"

I got there, there were probably 100 patients in the emergency side, which was only meant to hold 25.

Mark: I imagine that was incredibly hard for you to be separated from your family while they were going through it. Was this during your first of second time working in New York?

Jang Mi: It was in June 2020, my second trip. I was incredibly difficult to deal with, but I think it would have been different and even more difficult had their courses been more severe. They all did well and made complete recoveries.

Mark: Is it a relief to know that they have all had it?

Jang Mi: Yes and no. Because they are still cautious, they still wear masks because we still don't know if you can be re-infected. I read an article that the strain of coronavirus seen in Chicago is likely different from that in New York, indicating a difference between East and West coast cases. So, while we are learning more about the virus, there are still a lot of unknowns in terms of transmission, re-infection, and protection.

Mark: It would be interesting to know the answers to all those unknowns. Here in Utah, from my own observations, cases do seem to be different from those reported on the East coast. When you were home in Chicago, did you have to quarantine yourself from your family?

Jang Mi: Yes. I had to wear a mask in the house. We washed hands, but that is a normal habit for us anyway, so we didn't have to train anyone to wash their hands more frequently. I did try to stay at least 6 ft apart from them. It was hard because, you know, when you don't see your children for three weeks, they want to hug and hold onto you. Not being able to have that personal contact for so long was hard on all of us.

Mark: Yeah, that would be really hard. Where and/or how do you suspect they contracted the virus?

Jang Mi: I think they contracted the virus from not practicing social distancing. At the time, my husband, who works as a photographer, was going to peoples' homes to take portraits and although he did take precautions by wearing a respirator and conducting work outside as much as possible, he still had equipment and lighting to setup inside. So, I think he either acquired it from working in homes or many even just going to Costco back when masks weren't required to enter stores.

Mark: Tell us about your life and routine pre-pandemic and then leading up to working in New York.

Jang Mi: January 2020 was completely normal in terms of work and family life. In February 2020, I got the flu and I was very sick. I was out of the office for almost two weeks and came back to work at the end of February 2020. Before I went back to work, I was thinking about how the pandemic might impact work, how we would see patients and whether we had enough PPE required to provide physical care. The practice put suggested safety measures in place (e.g., asking patients to reschedule if they had fever or cough) and then everything shut down—clinical dermatology exams, general and cosmetic procedures—when the shelter-in-place order was passed.

Mark: It has all been absolutely crazy; science fiction-type situations we likely never thought we'd go through. When weighing the impact of providing care and being on frontlines during the coronavirus pandemic, do you personally feel that working in dermatology is equally impactful and fulfilling?

Jang Mi: I love dermatology. I love my patients. I've been working in the same practice for 12 years, so I have seen the same patient base for the past 12 years. We've been through life milestones together, graduations, careers, marriages, pregnancies, and welcoming new babies. It would be like leaving a family. If I left dermatology, I would miss those regular patients and dermatology patient interaction in general. I don't think working in the hospital center during the coronavirus pandemic has caused me to feel less fulfillment from dermatological care or view it as a less helpful/impactful specialty from a public health standpoint.

Mark: Are there any other cases from your time in New York that you feel are particularly illustrative of COVID-19 that might help people better understand the full picture?

Jang Mi: We did have a few patients who had the severe COVID-related symptoms with the cytokine storm and microemboli. I'm sure you have read a few articles about "COVID toes," but in all actuality, we saw patients who had COVID toes, feet, hands, and arms.

Mark: And are disseminated micro blood clots the cause of "COVID toes" presentation?

Jang Mi: Yes. There were some cases where we were constantly drawing blood from these patients because we were monitoring inflammatory markers and platelet counts—making sure our patients didn't actually have disseminated intravascular coagulation (DIC), another complication of COVID-19. I'll never forget this one patient I saw during my second trip working at Elmhurst while serving on the medical team. It was very difficult for the nursing staff to draw blood from this patient and, in the middle of the night, they called and said, "Hey, we can't get this blood. Can you guys [other team members] come down and try?" So we [myself and some other medicine team members] go down and found that this patient had absolutely no workable veins. You have a vein in your lower leg on the medial side where there should be superficial vessels that are well visualized and palpated. He had these vessels, but they were hard as a rock and you could not stick a needle in it. I ended up having to draw blood from the vessel in his index finger because that was the only location from which we could get the blood. As we were drawing the blood, it was clotting as it was going into the tubes and then just stop flowing altogether. At one time, we had to get an arterial stick because that was the best way to get blood. Even using the ultrasound to do an arterial stick, you could see the pulsations were very weak and even the blood coming out of the arterial vessel was almost black in color and had a tar-like consistency. To illustrate the unusualness of this detail, it is important to know that arterial blood is not supposed to be black nor is it supposed to be like tar. That incidence was the most frightening thing I've ever seen, and I'll probably have nightmares about it for a long time. I still have weird dreams about some of the patients seen during the pandemic.

Mark: I'm sure this has all has taken a huge toll on you mentally and emotionally.

Jang Mi: It has, and I don't think I've even been able to fully process all of it. When I returned home after the first trip to New York, some people asked how I dealt with it and I said, "Look, I've got to be honest with you. I don't think I've dealt with any of it yet."

So, I do yoga, read, and I try to meditate, but I think that there's going to be residual feelings that spontaneously surface. I am fully aware of the fragility of mental health and plan to seek professional counseling to work on processing my feelings.

Mark: Were those benefits available to you while onsite in New York?

Jang Mi: Yes. We had crisis counselors there in person at the hotel for a long time and then readily available via teleconference. I have to process all of this first before I can even understand how to help someone help me work through it.

Mark: I would guess that you are going to be processing it for a long time.

Jang Mi: Yeah, it's going to take a while but I'm going to make sure I get into a counseling program because I don't want this to affect me forever.

Mark: I can't imagine what you have been and continue to go through. As a friend and colleague of yours for many years, I want to say that I'm incredibly proud of you and thankful that you provided care not only during the time it was needed most, but in the area that was likely hardest hit. I think it's incredibly brave to do what you've done, and I know you well enough to guess that you probably don't even think much about serving, especially given gravity of the situation. It's all pretty amazing.

Jang Mi: Thanks. People say that to me, and I say, "thank you," but, you know, I don't think I deserve praise or gratitude because went home. The people who are employees at Elmhurst and other hospitals around the world caring for patients with COVID-19, this is where they live and work. They don't get to leave.

Mark: There's no end until it's really over.

Jang Mi: Right. So, I don't think I deserve any credit.

Mark: Well, you do deserve credit, but I also understand what you are saying about not living/working in what has been classified as the virus epicenters. I think that in some ways, from where I sit on the other side of the country, we were all able to benefit from the experiences and lessons learned in New York and we are all grateful to those who lived through it.

B. Jang Mi Johnson, PA-C, is a physician assistant at Dermio Dermatology in Munster, Indiana, and at V/O Med Spa River North, in Chicago, Illinois.

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

Address for Correspondence: *b.jangmijohnsonpa@gmail.com*

Part 2: West Coast pg. 40

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Dermatology Physicians Assistants Strong, Essential to COVID-19 Response Coast to Coast

PART 2: WEST COAST Spokane, WA— Employee Health Screening: A Different Frontline Experience for a Seasoned Derm PA

What was your initial reaction when you learned the coronavirus disease 2019 (COVID-19) was classified a pandemic?

TS: I remember hearing about the outbreak in China and was shocked by the number of people infected. At first, I thought it was probably containable. The next thing I know, there is a case in Seattle, Washington, in the same state where I reside! At that point, I knew coronavirus 1) was not contained and 2) was likely to be a devastating virus that would affect millions, including myself, my family, and friends.

Theresa Schimmels, PA-C, BCHS, DFAAPA

How did you become involved in the COVID-19 response?

TS: I work at a regional Veteran's Health Administration (VHA)/Veteran's hospital. As soon as the cases started to build in our state we "activated", so to speak. They asked for volunteers to help with different areas. Since I hadn't worked in a hospital or inpatient environment for over 20 years, I jumped on the first volunteer round to help Employee Health with screening services for hospital response. I was the secondary screener at the doors for two hours every morning and then assisted the doctor that runs employee health, who incredibly, was the medical director for the local PA program and whom I have known for at least 15 years. We knew we were a good team prior to all of this! Along with a couple of registered nurses, an administrative assistant, an advanced registered nurse practitioner (ARNP) volunteer like myself, a dental technician volunteer, we were the screening team. We were in charge of all COVID-19 screening, tracking, and implementing the Centers for Disease Control and Prevention (CDC) policies for who can and cannot be at work, how much time you have to take off, and we also order COVID testing as needed along with regular employee screening exams, recording accidents, and anything else related to employee health and welfare. I was involved in this group until earlier this month. Now I'm just backup if they need me as then carry on their duties.

How has your background as a respiratory therapist (RT) helped in the COVID response?

TS: I found my previous critical experience helped in understanding aspects of the physiological trauma that is often seen with this virus. I initially read about the "cytokine storm," the differences between patients with underlying lung conditions and so-called "normal" patients. I've read what this novel virus does to organ systems as well. I think my previous 15 years as a respiratory therapist (RT) helps me greatly in dermatology, too. I feel like it was the perfect pathway to becoming a PA since I worked office care for many years and can use all the immunology, rheumatology, and neurology I experience with my current patients. For example, I am aware of skin manifestations that co-occur with other conditions, such as rheumatic diseases, allergies, and movement disorders.

Does your history treating patients with human immunodeficiency viruses (HIV) echo what you are seeing now with COVID-19?

TS: Hmm. That's a good question. Maybe! Back then I was working in an inpatient environment and now I'm in an outpatient environment (and not brand new and "green" to medicine). My experiences have given me an appreciation for the unexpected. I treat everyone as if they may have something contagious. HIV turned out to be not as contagious as initially thought, thank goodness. COVID-19 is much more frightening because it is

so contagious. It's also "novel" and changing all the time; no one patient manifests the virus the same way. We are learning new things about it every day.

When did you enter the PA profession? Why Dermatology?

TS: I was encouraged to "do something more" by a group of pulmonologists I worked with in Spokane, Washington, where I live. Becoming a medical doctor or nurse practitioner (NP) meant I would have had to start all over in college; no one would recognize my previous degree. Then, all of a sudden, it seemed there were PAs working all over our multispecialty clinic, mostly prior service/military trained PAs. Their encouragement helped me research and discover that becoming a PA was the best route for me. I didn't want to be the doctor; I wanted to work with the team to provide care for those who faced barriers in getting access to care, and PAs did just that. After almost five years in primary care, I was fortunate enough to have a dermatologist who knew me when I was working as an RT. He invited me to work with him, helping to train me initially, with lots of precepting those first couple of years. And by adding me to his practice, we were able to continue to see Medicaid/Medicare and other underserved populations in our surrounding communities. I owe him a lot and we remain friends today. I moved to the VA in 2017. I've been in dermatology for 17 years now, and I'm passing that training on to the students I teach and precept as well as to the patients I see.

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Congratulations on being recognized by the University of Washington as an Outstanding PA and a Distinguished Lifetime Achievement Award winner. How do you feel about receiving the award?

Very honored and surprised to be receiving such an award. I have enjoyed being a PA more than I ever knew I would.

Did you realize when you were playing music in the Washington Air National Guard/AF band that you would enjoy your work serving Veterans so much?

Yes! I have always enjoyed experiences with patients who were Veterans or Active Duty military, both of which I have cared for throughout my career as my civilian clinic had a mission to serve our local military and military retiree community. I always hoped I could spend the last few years of my career at Mann-Grandstaff VAMC in Spokane, Washington, serving those who have served.

What is it about being a mentor/preceptor that you enjoy?

I really enjoy sharing my knowledge with students. There's a saying: See one-Do one-Teach one. My sharing experiences and approaches to caring for patients gives me an outlet to pass on what has been shared with me by other preceptors. Medicine and being a PA is a lifelong learning process. There's no better way to learn than to teach..

Any advice for young medical/PA students considering the career field?

Don't be afraid to try and then try again if you fail. Keep at it until you "get it," then keep learning more! Surround yourself with smart people and providers. By doing so, you'll learn a ton and will always have a place to share insights or ask questions.

What did you do in the military / which branch / years served?

I was in the Washington Air National Guard/AF for just over 20 years in the 560th AF Band/"Band of the Northwest" for my entire career, part of the 141 ARW at Fairchild AFB. I was officially the piano player but also played clarinet, oboe, percussion, and sang back up. Administratively, I was the PR/PA NCO and Band Operations NCO. It was a good career and a wonderful way to serve.

How long at VA? What do you like best about working here…?

I've been at the VA since 2017. I would say caring for Veterans is the best thing about working here. I am allowed more time to spend with each Veteran, giving them full focus on their medical issue rather than rushing them through to see the next patient. I also have a wonderful Dermatologist as my sponsoring physician, Dr

Marion Miethke. My staff including my nurse and the other providers and staff here have been really welcoming. I'd recommend it!

Theresa Schimmels, PA-C, BCHS, DFAAPA, *is a physician assistant at Mann-Grandstaff VA Medical Center in Spokane, Washington.*

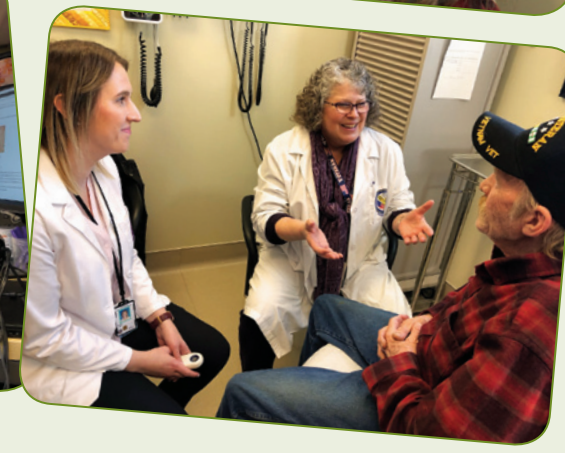
Disclosures: *The author has disclosed no potential conflicts of interest, financial or otherwise, relating to the content of this article.*

Address for Correspondence: *tmschimmels@gmail.com*

Read more about Theresa's achievements:

The Spokesman-Review https://www.spokesman.com/stories/2020/apr/21/front-lines-dermatology-specialist-who-cared-for-s/

UW Honors Spokane VA Physician Assistant https://www.spokane.va.gov/features/UW_Honors_Schimmels.asp



Certification Review

All Those Things Inside the Skin You Might Have Forgotten

By James A. Van Rhee, MS, PA-C

Are you recertifying soon? Start your board review early. Each issue of the JDPA features one board question accompanied by a brief explanation of the answer along with any pertinent test taking tips.Best of luck!

QUESTION: A 67-year-old female with a history of sarcoidosis, on chronic long-term immunosuppressants, presents for a routine health maintenance visit. She asks about updating her immunizations. All the following should be updated or administered in this patient **EXCEPT?**

A. Tetanus, diphtheria, pertussis (Tdap)
B. Influenza recombinant (RIV)
C. Pneumococcal (PPSV23)
D. Varicella (VAR)

EXPLANATION: The adult patient should have several immunizations updated on a regular basis. One dose of tetanus, diphtheria, pertussis (Tdap) should be given and then a Td or Tdap booster every ten years. Influenza recombinant (RIV) should be given annually. Pneumococcal polysaccharide (PPSV23) should be given as a single dose. Varicella (VAR) is contraindicated in patients who are immunocompromised since the vaccine contains live, attenuated virus. Other live vaccines given to adults include measles, mumps, rubella (MMR), smallpox, and yellow fever.

The correct answer is D.

James A. Van Rhee, MS, PA-C, *is the Program Director for the Yale University School of Medicine Physician Associate Program. Mr. Van Rhee has been involved in physician assistant education for over 20 years. He has served as project director and test item writer for the Physician Assistant Education Association's (PAEA) Physician Assistant Clinical Knowledge Rating Assessment Tool (PACKRAT). He is the author of the Physician Assistant: Certification and Re-certification Review Book and Consulting Editor of Physician Assistant Clinics, both published by Elsevier. For the last 15 years he has been course director and presenter of the Physician Assistant Board Review, produced live online by Kaplan Medical.*

Listening To Patients
The Joys of Telemedicine

By Alan Rockoff, MD

Another great morning, seeing patients in the comfort of quarantine!

Here goes. I'll invite Gretchen by text: 617-555-5555. "TOO LONG." How can 10 digits be too long?? Trying again: 617-555-5555. TOO LONG! What the heck, let me leave off the last digit: 617-555-555. "TOO SHORT."

Never mind, I'll invite her by email.

Five minutes have gone by. Better call to see if she got the invite.

"Hello, is this Gretchen? Don't hang up—I'm not a telemarketer! This is Dr. Rockoff. I sent you an invitation for our computer visit.

"You got it, great. Yes, you have to click on it to sign in. I know, your appointment is at 8:30. It's now 8:28. Let's start early, why not?

"Hi, there! I can see you. Can you hear me? You're nodding and your lips are moving. I can't hear you. Did you enable your microphone?

"Nope, still can't hear. I'll call your cell, and we'll talk that way.

"Yes, it's me, Dr. Rockoff. What's that? You enabled the microphone along with your video when you logged on? Well, there you go. How can I help today?

"You want a refill on your tretinoin gel for age management? Not a problem. Let's see, you've been using it since 1996. No, you look great! Not a day over 76, really! I'll have the staff escribe it right over.

"Okay, take care. Three years should be about right. Happy 80th!"

Wonder what happened there. Maybe things will go better for the next patient. Okay, I'm emailing an invite to Rob.

There he is! "Hi. Can you see me? Hear me? Nope, can't hear you. Let me just call your cell."

OK, 972-555-5555. Ringing….oh no, right to voicemail. "You have reached 972-555-5555. The mailbox is full and cannot accept messages. Please try some other time."

"Okay, I'm back with you on the screen, Rob. Nope, still can't hear you. I tried your cell but it went to voicemail. Yes, I see you're holding the phone in your hand. Let me try you again.

"972-555-5555. Right to voicemail. Doesn't your phone ring? You never make voice calls, only send texts? Look, please call me: 781-555-5555, write it down.

"Excellent, we're in business. You're worried about a mole that's changing. You sent a photo to the office. Great, I'll look right now on your record….nope, not uploaded. Can you email me the photo? Please write down my email address: alanrockoffmdskincarespecialist@myfabuloustelemedicineportal.now. Got that? Ok, please send the picture…..

"Returned as undeliverable? Show me what you typed….Oh, wait. It's 'telemedicine,' not 'TellaMedicine.' Yeah, that should do it.

"OK, got the picture. You do fabulous super-closeups! Is that your navel next to it? Your left nostril? OK. You tried to razor off the hair growing out it? Yes, that could account for the bleeding. Tell you what, go easy on it for the next two weeks, and send me another picture. Same email address.

"You have another question? Sure. You want a refill of your clindamycin gel because the tube from 2013 ran out? Guess you haven't grown out of your acne yet. Sure, happy to send it in for you. Same pharmacy we have on file? You're bunking with your parents in Wichita? No problem. Just need the pharmacy name and street. Boston, Wichita, whichever.

"Sure, happy to help. Enjoy your stay with your parents. You've been there four months? Are you cleaning your room? Mostly? Good. Take care. I'll respond to your email in two

weeks. Meantime, you might empty out your full voicemail box….Oh, right, your generation only texts…."

OK, one more. Here's Henrietta. I emailed her an invitation…Holy Cow, she's checked in! Let's see, click "Join". I can see her!

"Henrietta, is that you? Can you hear me? You can??!! You can hear me! Henrietta can hear me! And I can hear her!

"Yes, Henrietta, I'm all right. Just doing cartwheels around my study. Between COVID and the 95 degree heat and 100% humidity, it's all the exercise I get.

"How can I help you today?

"Henrietta? HENRIETTA! Where have you gone, Henrietta?"

THERE IS A PROBLEM WITH YOUR CALL. DISCONNECT YOUR ROUTER, WAIT 65 SECONDS, RECONNECT, THEN RESTART YOUR WIFI, AND LOG IN AGAIN.

Maybe it's time to go back to the office. A face shield and HAZMAT suit are sounding better all the time…

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.

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https://www.mdedge.com/dermatology/article/227793/business-medicine/joys-telemedicine
Accessed September 23, 2020.)
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A NOVEL ORAL TETRACYCLINE DEVELOPED SPECIFICALLY FOR MODERATE TO SEVERE ACNE IN PATIENTS AS YOUNG AS 9[1]

* With spontaneous mutation frequencies being 10^{-10} at 4–8 × MIC.[1]

† **STUDY DESIGN:** The safety and efficacy of SEYSARA was assessed in two identically designed, 12-week, multicenter, randomized, double-blind, placebo-controlled trials. In both studies, SEYSARA was administered orally once daily for 12 weeks as 60-mg, 100-mg, or 150-mg tablets, based on patient weight. **STUDY RESULTS:** Mean absolute reduction (co-primary endpoint) was 15.3 in study 1 (SC1401) and 15.5 in study 2 (SC1402) vs 10.2 and 11.1 in the placebo groups at Week 12, respectively. Overall, 21.9% of ITT patients in study 1 and 22.6% of ITT patients in study 2 achieved IGA success (co-primary endpoint), defined as ≥2-point improvement from baseline in IGA scale for inflammatory lesions of acne and a score of 0 (clear) or 1 (almost clear), at Week 12 vs 10.5% and 15.3% of patients with placebo, respectively ($P < .0001$ for study 1 and $P = .0038$ for study 2).

INDICATIONS AND USAGE

SEYSARA (sarecycline) tablet, is indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older.

Limitations of Use: Efficacy of SEYSARA beyond 12 weeks and safety beyond 12 months have not been established. SEYSARA has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, SEYSARA should be used only as indicated.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

SEYSARA is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines.

WARNINGS AND PRECAUTIONS

- Like other tetracyclines, SEYSARA can cause fetal harm when administered to a pregnant woman. If SEYSARA is used **during pregnancy**, or if the patient becomes pregnant while taking SEYSARA, the patient should be informed of the potential hazard to the fetus and treatment should be stopped immediately.
- The use of SEYSARA during **tooth development** (second and third trimesters of pregnancy, infancy, and childhood up to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown).
- ***Clostridium difficile* associated diarrhea (CDAD)** has been reported with nearly all antibacterial agents, and may range in severity from mild diarrhea to fatal colitis. If *Clostridium difficile* Associated Diarrhea (antibiotic associated colitis) occurs, discontinue SEYSARA.
- **Central nervous system side effects,** including light-headedness, dizziness or vertigo, have been reported with tetracycline use. Patients who experience these symptoms should be cautioned about driving vehicles or using hazardous machinery. These symptoms may appear during therapy and may disappear when the drug is discontinued.

SEYSARA:
AN ORAL ANTIBIOTIC THAT'S ON TARGET FOR ACNE

LOW ANTIBIOTIC RESISTANCE IN ACNE

- *Propionibacterium acnes* strains displayed a low propensity for the development of resistance to sarecycline[1,2*]
- Sarecycline is active *in vitro* against most isolates of *P. acnes*; however, the clinical significance is unknown[1]

PROVEN EFFICACY IN FACIAL AND TRUNCAL ACNE

- Significant inflammatory lesion count reduction on the face at Week 12 and as early as Week 3[1†]
- The only oral antibiotic for acne with significant facial and truncal efficacy data[3†]

SAFETY AND TOLERABILITY DATA UP TO 12 MONTHS[4]

- An established safety profile with low rates of GI, vestibular, and phototoxic side effects[1-3]
- The most common adverse reaction in pivotal trials was nausea (incidence ≥1%)[1]

Please see *Limitations of Use* and *Warnings and Precautions* regarding bacterial resistance below

CHOOSE SEYSARA: THE ONE AND ONLY ORAL ANTIBIOTIC DEVELOPED SPECIFICALLY FOR ACNE

- **Intracranial hypertension** in adults and adolescents has been associated with the use of tetracyclines. Clinical manifestations include headache, blurred vision and papilledema. Although signs and symptoms of intracranial hypertension resolve after discontinuation of treatment, the possibility for sequelae such as visual loss that may be permanent or severe exists. Concomitant use of isotretinoin and SEYSARA should be avoided because isotretinoin, a systemic retinoid, is also known to cause intracranial hypertension.
- **Photosensitivity** manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using SEYSARA.
- **Bacterial resistance** to tetracyclines may develop in patients using SEYSARA. Because of the potential for drug-resistant bacteria to develop during the use of SEYSARA, it should only be used as indicated.
- As with other antibiotic preparations, use of SEYSARA may result in overgrowth of non-susceptible organisms, including fungi. If **superinfection** occurs, SEYSARA should be discontinued and appropriate therapy instituted.

ADVERSE REACTIONS

Most common adverse reaction (incidence ≥1%) is nausea.

Please turn the page for Brief Summary of full Prescribing Information.

GI, gastrointestinal; IGA, investigator's global assessment; ITT, intent-to-treat; MIC, minimum inhibitory concentration.

References:

1. SEYSARA [package insert]. Exton, PA: Almirall, LLC, 2020.
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US-SEY-2000142 10-2020

almirall

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION FOR SEYSARA® (sarecycline)

This brief summary does not include all the information needed to use SEYSARA safely and effectively. See full Prescribing Information for SEYSARA (sarecycline) tablets for oral use.

INDICATIONS AND USAGE

SEYSARA® (sarecycline) tablet, is indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older.

Limitations of Use: Efficacy of SEYSARA beyond 12 weeks and safety beyond 12 months have not been established. SEYSARA has not been evaluated in the treatment of infections.

To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, SEYSARA should be used only as indicated *[see Warnings and Precautions].*

CONTRAINDICATIONS

SEYSARA is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines.

WARNINGS AND PRECAUTIONS

Teratogenic Effects

- SEYSARA, like other tetracyclines, can cause fetal harm when administered to a pregnant woman. If SEYSARA is used during pregnancy or if the patient becomes pregnant while taking SEYSARA, the patient should be informed of the potential hazard to the fetus and treatment should be stopped immediately.
- The use of drugs of the tetracycline-class during tooth development (second and third trimesters of pregnancy, infancy, and childhood up to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). This adverse reaction is more common during long-term use of these drugs, but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported.
- All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature human infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued. Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development on the developing fetus. Evidence of embryotoxicity has been noted in animals treated with SEYSARA during pregnancy in association with maternal toxicity *[see Use in Specific Populations]*.

***Clostridium difficile* Associated Diarrhea (Antibiotic Associated Colitis)**

Clostridium difficile associated diarrhea (CDAD) has been reported with nearly all antibacterial agents, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to potential overgrowth of *C. difficile.*

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* should be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Central Nervous System Effects

Central nervous system side effects including light-headedness, dizziness or vertigo have been reported with tetracycline use. Patients who experience these symptoms should be cautioned about driving vehicles or using hazardous machinery. These symptoms may disappear during therapy and may disappear when the drug is discontinued.

Intracranial Hypertension

Intracranial hypertension in adults and adolescents has been associated with the use of tetracyclines. Clinical manifestations include headache, blurred vision and papilledema. Although signs and symptoms of intracranial hypertension resolve after discontinuation of treatment, the possibility for sequelae such as visual loss that may be permanent or severe exists. Women of childbearing age who are overweight have a greater risk for developing intracranial hypertension. Patients should be questioned for visual disturbances prior to initiation of treatment with tetracyclines. Concomitant use of isotretinoin and SEYSARA should be avoided because isotretinoin, a systemic retinoid, is also known to cause intracranial hypertension *[see Drug Interactions]*. If visual disturbance occurs during treatment, patients should be checked for papilledema.

Photosensitivity

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using SEYSARA. If patients need to be outdoors while using SEYSARA, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician.

Development of Drug Resistant Bacteria

Bacterial resistance to tetracyclines may develop in patients using SEYSARA. Because of the potential for drug-resistant bacteria to develop during the use of SEYSARA, it should only be used as indicated.

Superinfection/Potential for Microbial Overgrowth

As with other antibiotic preparations, use of SEYSARA may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, SEYSARA should be discontinued and appropriate therapy instituted.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

A total of 1064 subjects and 1069 subjects with moderate to severe acne vulgaris were treated with SEYSARA and placebo, respectively, for 12 weeks in 3 controlled clinical trials. The only adverse drug reaction that was reported in at least 1% of subjects was nausea, SEYSARA (3.1%) versus placebo (2.0%).

The following additional adverse drug reactions occurred in less than 1% of female SEYSARA subjects: vulvovaginal mycotic infection (0.8%) and vulvovaginal candidiasis (0.6%).

DRUG INTERACTIONS

Effect of Other Drugs on SEYSARA

Oral Retinoids: Tetracyclines may cause increased intracranial pressure as do oral retinoids, including isotretinoin and acitretin *[see Warnings and Precautions]*. Avoid coadministration of SEYSARA with oral retinoids.

Antacids and Iron Preparations: Coadministration with antacids containing aluminum, calcium or magnesium, bismuth subsalicylate, and iron-containing preparations may impair absorption of SEYSARA, similar to other tetracyclines, which may decrease its efficacy. Separate dosing of SEYSARA from antacids containing aluminum, calcium or magnesium, bismuth subsalicylate, and iron-containing preparations.

Effect of SEYSARA on Other Drugs

Penicillin: Similar to other tetracyclines, SEYSARA may interfere with the bactericidal action of penicillin. Avoid coadministration of SEYSARA with penicillin.

Anticoagulants: Similar to other tetracyclines, SEYSARA may depress plasma prothrombin activity, which may increase the risk of bleeding in patients who are on anticoagulant therapy. Decrease anticoagulant dosage when coadministered with SEYSARA as appropriate.

P-Glycoprotein (P-gp) Substrates: Concomitant use of SEYSARA may increase concentrations of concomitantly administered P-gp substrates (e.g. digoxin). Monitor for toxicities of drugs that are P-gp substrates and may require dosage reduction when given concurrently with SEYSARA.

Oral Hormonal Contraceptives: There is no clinically significant effect of SEYSARA on the efficacy of oral contraceptives containing ethinyl estradiol and norethindrone acetate.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary: SEYSARA, like tetracycline class drugs, may cause fetal harm, permanent discoloration of teeth, and reversible inhibition of bone growth when administered during pregnancy *[see Warnings and Precautions and Use in Specific Populations]*. The limited available human data are not sufficient to inform a drug-associated risk for birth defects or miscarriage. Tetracyclines are known to cross the placental barrier; therefore, SEYSARA may be transmitted from the mother to the developing fetus. In animal reproduction studies, sarecycline induced skeletal malformations in fetuses when orally administered to pregnant rats during the period of organogenesis at a dose 1.4 times the maximum recommended human dose (MRHD) of 150 mg/day (based on AUC comparison). When dosing with sarecycline continued through the period of lactation, decreases in offspring survival, offspring body weight, and implantation sites and viable embryos in offspring females occurred at a dose 3 times the MRHD (based on AUC comparison). The potential risk to the fetus outweighs the potential benefit to the mother from SEYSARA use during pregnancy; therefore, pregnant patients should discontinue SEYSARA as soon as pregnancy is recognized.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Lactation

Risk Summary: Tetracyclines are excreted in human milk. Because of the potential for serious adverse reactions on bone and tooth development in nursing infants from tetracycline-class antibiotics, advise a woman that breastfeeding is not recommended with SEYSARA therapy *[see Warnings and Precautions]*.

Females and Males of Reproductive Potential

Infertility: Avoid using SEYSARA in males who are attempting to conceive a child. In a fertility study in rats, sarecycline adversely affected spermatogenesis when orally administered to male rats at a dose 8 times the MRHD (based on AUC comparison).

Pediatric Use

The safety and effectiveness of SEYSARA have been established in pediatric patients 9 years of age and older for the treatment of moderate to severe inflammatory lesions of non-nodular acne vulgaris.

Safety and effectiveness of SEYSARA in pediatric patients below the age of 9 years has not been established. Use of tetracycline-class antibiotics below the age of 8 is not recommended due to the potential for tooth discoloration *[see Warnings and Precautions]*.

Geriatric Use

Clinical studies of SEYSARA did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

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Gluteal Hidradenitis Suppurativa Presenting Pemphigus-Like Findings: Case Report

Yuichi Kurihara[1] and Masutaka Furue[2]*

[1]*Department of Dermatology, Steel Memorial Yawata Hospital, 1-1-1 Harunomachi, Yahatahigashi-ku, Kitakyushu 805-8508, Japan.*
[2]*Department of Dermatology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan*

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ABSTRACT

Background: Hidradenitis suppurativa is one member of the follicular occlusion triad: acne conglobata, hidradenitis suppurativa, and dissecting cellulitis of the scalp. The presence of acantholysis and desmoglein autoantibodies in hidradenitis suppurativa is rare.

Case presentation: We report a case of 68-year-old male with a diagnosis of gluteal hidradenitis suppurativa copresenting pemphigus-like findings including acantholysis and positive desmoglein autoantibodies.

Conclusion: To our knowledge, comorbidity of gluteal hidradenitis suppurativa and pemphigus-like findings has not been reported before. This case implies a relationship between two different conditions; the follicular occlusion triad and pemphigus, highlighting a potential induction of pemphigus-like lesion by chronic inflammatory process.

KEYWORDS

Hidradenitis suppurativa, Pemphigus, Acantholysis, Desmoglein autoantibodies

BACKGROUND

Hidradenitis suppurativa is one member of the follicular occlusion triad: acne conglobata, hidradenitis suppurativa, and dissecting cellulitis of the scalp.[1] This group of conditions presents with deep scarring folliculitis composed of multichannel draining sinus and abscesses.[1] Hidradenitis suppurativa is a progressive inflammatory disease and emerges comorbid autoimmune disease.[2] We report a rare case of gluteal hidradenitis suppurativa which also presented acantholysis and desmoglein autoantibodies.

CASE PRESENTATION

A 68-year-old male presented slightly tender brown nodules and purulent discharge on the right thigh. There were no evident blisters or erosions. He had first developed these lesions three years previously and they had been gradually enlarged. Physical examination revealed brown nodules, multiple fistulae, and scars on the right side of the thigh *(Fig. 1a)*. No other areas of the body including mucosal areas were affected. The patient did not report any gastrointestinal symptoms and had no remarkable past

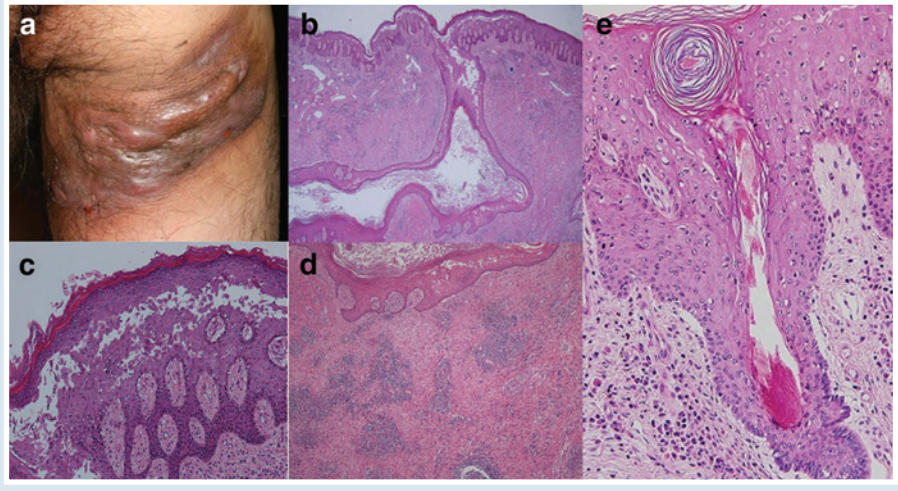

Fig. 1 ***(a)*** *Brown nodules, multiple fistula and scars on the right side of the thigh.*
(b) *Clefts and acantholysis in the epidermis (hematoxylin and eosin, original magnification × 40).*
(c) *Presence of intraepidermal acantholytic cells (original magnification × 200)*
(d) *Abscesses and chronic inflammation in the upper dermis. (hematoxylin and eosin, original magnification × 100).*
(e) *Involvement of hair follicle in the lesion (original magnification × 200)*

medical history including immunodeficiency and relevant family history. Staphylococcus aureus was cultured from the lesion but oral antibiotic treatment for over three months was ineffective, then surgical removal of the lesion was performed. The whole lesion had been totally excised and processed for formalin-fixation. Therefore, standard direct immunofluoresence test was not performed. Indirect immunofluorescence finding was negative. The results of serum ELISA tests for anti-desmoglein 1 and 3 (MESACUP desmoglein 1 and desmoglein 3, MBL) were positive (ELISA titers were 36 and 11, respectively) and epidermal hyperplasia, numerous intraepidermal clefts and acantholysis were demonstrated in histology *(Fig. 1b, c)*. Furthermore, the findings of gluteal hidradenitis suppurativa, namely, multiple sinus tracts, abscesses, chronic inflammation with polymorphonuclear leukocytes and lymphocytes, and follicle-based inflammation were observed *(Fig. 1d, e)*. Considering the age of onset, unilaterality of lesion and the site and extent of lesion, hidradenitis suppurativa was compatible rather than acne conglobata. At the time of writing, no signs of recurrence after the surgical treatment have emerged.

The differential diagnosis includes pyoderma vegetans, pemphigus vegetans, pyodermatitis-pyostomatitis and other autoimmune blistering dermatoses. In the present case, the absence of mucosal lesions, abdominal symptoms, and eosinophilia ruled out the diagnosis of pyoderma vegetans and pyodermatitis-pyostomatitis. The response to oral antibiotics was poor and ruled out infected pemphigus vegetans. We diagnosed this case as hidradenitis suppurativa with pemphigus-like findings because of the unilaterally-localized lesion, low titer of desmoglein antibodies and negative indirect immunofluorescence finding, although concomitant presence of hidradenitis suppurativa and pemphigus could not be ruled out exactly.

DISCUSSION AND CONCLUSION

Although the precise pathogenesis is not fully understood, a previous study described the pemphigus-pyoderma spectrum.[3] The present case also suggests a potential (at least coincidental) relationship between the follicular occlusion triad and pemphigus-like findings. Interestingly, although the blood test results were positive for IgG antibody to desmoglein 1 and 3, the lesion was confined to the thigh. A previous report indicated the association between recurrent staphylococcal infection and the development of an anti-desmoglein 3 antibody response.[4,5] It was possible that recurrent bacterial infections may influence or aggravate the intraepidermal lesions in the present case. Finally, the present case may highlight a possibility that pemphigus-like findings can be triggered or induced by chronic inflammatory process like hidradenitis suppurativa.

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Authors' contributions
YK was involved in the conception of the work, the acquisition of data and drafted the work. MF was involved in the design of the work, the analysis of data and revising the manuscript. All authors have read and approved the manuscript.

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Availability of data and materials
All data is included within the published article.

Ethics approval and consent to participate
Not applicable.

Consent for publication
The patient gave written informed consent to the publication of the case report, including clinical details and images. A copy of the written informed consent is available for review by the Editor of this journal if requested.

Competing interests
The authors declared that they have no competing interests.

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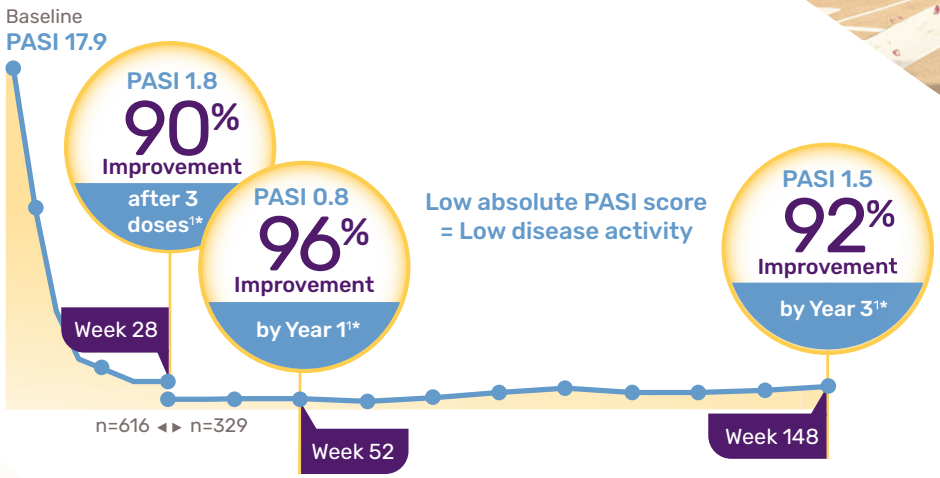
** Correspondence: yukuri549@gmail.com*
[1]Department of Dermatology, Steel Memorial Yawata Hospital, 1-1-1 Harunomachi, Yahatahigashi-ku, Kitakyushu 805-8508, Japan

In moderate-to-severe plaque psoriasis

CONSISTENT, LONG-TERM CLEARANCE[1]*

MEDIAN ABSOLUTE PASI SCORE RAPIDLY REDUCED AND SUSTAINED THROUGH YEAR 3[1]*



ILUMYA™
tildrakizumab-asmn
Injection 100 mg/mL

Co-primary endpoints: PGA 0/1 with at least a 2-point improvement, and PASI 75, both at Week 12[2]

- **After 2 doses**, by Week 12, 58% (reSURFACE 1) and 55% (reSURFACE 2) achieved PGA 0/1
  - vs placebo: 7% (reSURFACE 1) and 4% (reSURFACE 2)
- **After 2 doses**, by Week 12, 64% (reSURFACE 1) and 61% (reSURFACE 2) achieved PASI 75
  - vs placebo: 6% (reSURFACE 1) and 6% (reSURFACE 2)

At Week 28, responders were re-randomized to 100 mg, 200 mg, or treatment withdrawal, and non-responders (14.4%) were discontinued from therapy. Data represents recommended 100 mg group.[1,2]

*From a pooled analysis of reSURFACE 1 and 2. Conducted with non-responder imputation. View study design for reSURFACE 1 and 2 at ILUMYApro.com/results.

PASI=Psoriasis Area and Severity Index; PGA=Physician Global Assessment.

See more long-term results at **ILUMYAdurability.com**

Watch data highlights video

INDICATION

ILUMYA™ (tildrakizumab-asmn) is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ILUMYA™ is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity
Cases of angioedema and urticaria occurred in ILUMYA™-treated subjects in clinical trials. If a serious allergic reaction occurs, discontinue ILUMYA™ immediately and initiate appropriate therapy.

Infections
ILUMYA™ may increase the risk of infection. Treatment with ILUMYA™ should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated.

Consider the risks and benefits of treatment prior to prescribing ILUMYA™ in patients with a chronic infection or a history of recurrent infection. Instruct patients receiving ILUMYA™ to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection, or is not responding to standard therapy, closely monitor and consider discontinuation of ILUMYA™ until the infection resolves.

Pretreatment Evaluation for Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with ILUMYA™. Do not administer ILUMYA™ to patients with active TB infection. Initiate treatment of latent TB prior to administering ILUMYA™. Consider anti-TB therapy prior to initiation of ILUMYA™ in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving ILUMYA™ should be monitored closely for signs and symptoms of active TB during and after treatment.

Immunizations
Prior to initiating therapy with ILUMYA™, consider completion of all age-appropriate immunizations according to current immunization guidelines. Patients treated with ILUMYA™ should not receive live vaccines.

Adverse Reactions
The most common (≥1%) adverse reactions associated with ILUMYA™ treatment that were more frequent than in the placebo group are upper respiratory infections, injection-site reactions, and diarrhea.

Please see Brief Summary of Prescribing Information on the following page.

References: 1. Data on File. Sun Pharmaceutical Industries, Inc. **2.** ILUMYA™ [package insert]. Princeton, NJ: Sun Pharmaceutical Industries, Inc.

SUN DERMATOLOGY

Brief Summary of Prescribing Information for ILUMYA™ (tildrakizumab-asmn)
ILUMYA™ (tildrakizumab-asmn) injection, for subcutaneous use
See package insert for full Prescribing Information

INDICATIONS AND USAGE ILUMYA™ is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

CONTRAINDICATIONS
ILUMYA is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS
Hypersensitivity: Cases of angioedema and urticaria occurred in ILUMYA treated subjects in clinical trials. If a serious hypersensitivity reaction occurs, discontinue ILUMYA immediately and initiate appropriate therapy *[see Adverse Reactions]*.

Infections: ILUMYA may increase the risk of infection. Although infections were slightly more common in the ILUMYA group (23%), the difference in frequency of infections between the ILUMYA group and the placebo group was less than 1% during the placebo-controlled period. However, subjects with active infections or a history of recurrent infections were not included in clinical trials. Upper respiratory infections occurred more frequently in the ILUMYA group than in the placebo group *[see Adverse Reactions]*.

The rates of serious infections for the ILUMYA group and the placebo group were ≤0.3%. Treatment with ILUMYA should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing ILUMYA. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard therapy, monitor the patient closely and consider discontinuation of ILUMYA until the infection resolves *[see Adverse Reactions]*.

Pretreatment Evaluation for Tuberculosis: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with ILUMYA. Initiate treatment of latent TB prior to administering ILUMYA. In clinical trials, of 55 subjects with latent TB who were concurrently treated with ILUMYA and appropriate TB prophylaxis, no subjects developed active TB (during the mean follow-up of 56.5 weeks). One other subject developed TB while receiving ILUMYA. Monitor patients for signs and symptoms of active TB during and after ILUMYA treatment. Consider anti-TB therapy prior to initiation of ILUMYA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Do not administer ILUMYA to patients with active TB infection.

Immunizations: Prior to initiating therapy with ILUMYA, consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid the use of live vaccines in patients treated with ILUMYA. No data are available on the response to live or inactive vaccines.

ADVERSE REACTIONS
The following serious adverse reactions are discussed elsewhere in the labeling:
Hypersensitivity Reactions *[see Warnings and Precautions]*
Infections *[see Warnings and Precautions]*

Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, a total of 1994 subjects with plaque psoriasis were treated with ILUMYA, of which 1083 subjects were treated with ILUMYA 100 mg. Of these, 672 subjects were exposed for at least 12 months, 587 for 18 months, and 469 for 24 months.

Data from three placebo-controlled trials (Trials 1, 2, and 3) in 705 subjects (mean age 46 years, 71% males, 81% white) were pooled to evaluate the safety of ILUMYA (100 mg administered subcutaneously at Weeks 0 and 4, followed by every 12 weeks [Q12W]) *[see Clinical Studies]*.

Placebo-Controlled Period (Weeks 0-16 of Trial 1 and Weeks 0-12 of Trials 2 and 3)
In the placebo-controlled period of Trials 1, 2, and 3 in the 100 mg group, adverse events occurred in 48.2% of subjects in the ILUMYA group compared to 53.8% of subjects in the placebo group. The rates of serious adverse events were 1.4% in the ILUMYA group and 1.7% in the placebo group.

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the ILUMYA group than in the placebo group.

Table 1: Adverse Reactions Occurring in ≥1% of Subjects in the ILUMYA Group and More Frequently than in the Placebo Group in the Plaque Psoriasis Trials 1, 2, and 3

Adverse Reaction	ILUMYA 100 mg (N=705) N (%)	Placebo (N=355) N (%)
Upper respiratory infections*	98 (14)	41 (12)
Injection site reactions†	24 (3)	7 (2)
Diarrhea	13 (2)	5 (1)

* Upper respiratory infections include nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, and pharyngitis.

† Injection site reactions include injection site urticaria, pruritus, pain, reaction, erythema, inflammation, edema, swelling, bruising, hematoma, and hemorrhage.

During the placebo-controlled period of Trials 1, 2, and 3, adverse reactions that occurred at rates less than 1% but greater than 0.1% in the ILUMYA group and at a higher rate than in the placebo group included dizziness and pain in extremity.

Specific Adverse Reactions
Hypersensitivity Reactions
Cases of angioedema and urticaria occurred in ILUMYA-treated subjects in clinical trials *[see Warnings and Precautions]*.

Infections
Infections were slightly more common in the ILUMYA group. The difference in frequency of infections between the ILUMYA group (23%) and the placebo group was less than 1% during the placebo-controlled period. The most common (≥1%) infections were upper respiratory infections. The rates of severe infections for the ILUMYA group and the placebo group were ≤0.3%.

Safety Through Week 52/64
Through Week 52 (Trials 1 and 3) and Week 64 (Trial 2), no new adverse reactions were identified with ILUMYA use and the frequency of the adverse reactions was similar to that observed during the placebo-controlled period.

Immunogenicity
As with all therapeutic proteins there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to tildrakizumab in the studies described below with the incidences of antibodies in other studies or to other products may be misleading.

Up to Week 64, approximately 6.5% of subjects treated with ILUMYA 100 mg developed antibodies to tildrakizumab. Of the subjects who developed antibodies to tildrakizumab, approximately 40% (2.5% of all subjects receiving ILUMYA) had antibodies that were classified as neutralizing. Development of neutralizing antibodies to tildrakizumab was associated with lower serum tildrakizumab concentrations and reduced efficacy.

DRUG INTERACTIONS
Live Vaccinations
Avoid use of live vaccines in patients treated with ILUMYA *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS
Pregnancy: Risk Summary
Limited available data with ILUMYA use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes. Human IgG is known to cross the placental barrier; therefore, ILUMYA may be transferred from the mother to the fetus. An embryofetal developmental study conducted with tildrakizumab in pregnant monkeys revealed no treatment-related effects to the developing fetus when tildrakizumab was administered subcutaneously during organogenesis to near parturition at doses up to 159 times the maximum recommended human dose (MRHD). When dosing was continued until parturition, a small increase in neonatal death was observed at 59 times the MRHD *[see Data]*. The clinical significance of this nonclinical finding is unknown.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data: *Animal Data*
In an embryofetal developmental study, subcutaneous doses up to 300 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks during organogenesis to gestation day 118 (22 days from parturition). No maternal or embryofetal toxicities were observed at doses up to 300 mg/kg (159 times the MRHD of 100 mg, based on AUC comparison). Tildrakizumab crossed the placenta in monkeys.

In a pre- and postnatal developmental study, subcutaneous doses up to 100 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks from gestation day 50 to parturition. Neonatal deaths occurred in the offspring of one control monkey, two monkeys at 10 mg/kg dose (6 times the MRHD based on AUC comparison), and four monkeys at 100 mg/kg dose (59 times the MRHD based on AUC comparison). The clinical significance of these nonclinical findings is unknown. No tildrakizumab-related adverse effects were noted in the remaining infants from birth through 6 months of age.

Lactation: Risk Summary
There are no data on the presence of tildrakizumab in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG is known to be present in human milk. Tildrakizumab was detected in the milk of monkeys *[see Data]*.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ILUMYA and any potential adverse effects on the breastfed child from ILUMYA or from the underlying maternal condition.

Pediatric Use: Safety and effectiveness of ILUMYA in pediatric patients (<18 years of age) have not been established.

Geriatric Use: A total of 1083 subjects were exposed to ILUMYA 100 mg during Phase 2 and 3 trials. A total of 92 subjects were 65 years or older, and 17 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 and over is not sufficient to determine whether they respond differently from younger subjects.

OVERDOSAGE: In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and administer appropriate symptomatic treatment immediately.

PATIENT COUNSELING INFORMATION: Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide).

Instruct patients and/or caregivers to read the Medication Guide before starting ILUMYA therapy and to reread the Medication Guide each time the prescription is renewed. Advise patients of the potential benefits and risks of ILUMYA.

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INFORMATION FOR AUTHORS

JDPA
Journal of Dermatology for Physician Assistants

The official journal of the Society of Dermatology Physician Assistants

JOURNAL OVERVIEW

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

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

EDITORIAL MISSION

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

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

CONTENT FOCUS

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

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

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

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

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

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Reference Formatting Guide

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

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

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

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

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

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- ***Continuing Education (CME).*** Content should be specific to the field of dermatology following any of the following formats: Original research (clinical or basic science), Professional issues or health policy papers, Scholarly review of a topic. **Recommended content length:** up to 5,000 words not including references. **Requirements:** Learning Objectives (4), Statement explaining how the article addresses practice gaps, and Self-assessment post-test questions (4).
- ***Dermatology Case Report.*** Discuss a case(s) that illustrates an important or interesting observation. Cases should stimulate research and the exchange of information and illustrate the signs and symptoms, diagnosis, and treatment of a dermatological condition. At least 15 current references are recommended. Illustrative material is preferred. Must include abstract. (1,000 to 3,000 words).
- ***Clinical Dermatology PA Perspectives.*** A review of published article summarizing the practical thoughts and clinical issues (250-1000 words).
- ***From the Patient's Perspective.*** Patients' stories published in their own words. JDPA staff can even assist patients with writing their stories (250-1000 words).
- ***Clinical Snapshots.*** A brief written description and clinical facts about an interesting cutaneous anomaly (250-500 words).
- ***Drugs in Dermatology.*** Write about the current information regarding a particular dermatological medication, drug interaction, or medication side effect/adverse reaction (250-1000 words).
- ***Dermatology Evidence-Based Medicine (derm EBM).*** A brief, evidence-based assessment of the one or two most relevant studies retrieved to answer a focused clinical question that may have arisen from a real-life situation. A derm EBM is not a comprehensive review of a subject or a synthesis of all the available knowledge (500–1500 words).

COSMETIC DERMATOLOGY

- ***Feature Articles***. A review about a new or innovative cosmetic procedure, device, and/or approach to patient care (500-1000 words).
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- ***Cosmetic Dermatology Case Report.*** Write a report and discuss a case(s) that illustrate an important or interesting observation (500-1500 words).
- ***Cosmetic Dermatology PA Perspectives.*** Write a review of published article summarizing the practical thoughts and clinical issues (250-1000 words).

COSMETIC DERMATOLOGY

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- ***Feature Articles***. A review of a new or innovative dermatological procedure, device, and/or approach to patient care (500-1000 words).
- ***From The Desk Of…***Write an opinion essay sharing your insight regarding a current "hot item" issue (e.g., specialty PA credentialing, dermatology access to care, supervising physician relationships, etc.) or any other topic regarding the field of dermatology (250-1000 words).

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- ***Feature Articles.*** An article that explores the professional issues dermatology PAs face, such as reimbursement, education, medical trends, contracts, office management, etc. (500-1500 words).
- ***Outside & Inside the 9 to 5***. Share your story of the good work that you do either outside or inside your practice of dermatology. (250-1000 words).
- ***Notes From Your Office Manager***. A brief article on a fact or pearl for the office setting (250-500 words).
- ***Judicial and Ethical Affairs.*** An article that explores the complex or multifaceted ethical or judicial professional issues that affect the practice of dermatology for PAs (250-1000 words).

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

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All submissions must adhere to the following format:

- Main Submission Document prepared in Microsoft Word (no PDFs) or similar word processing program
- Font: Times New Roman font, size 12, black
- Formatting: Use double spacing throughout
- Do not include footnotes within the manuscript body
- All abbreviations and acronyms should be spelled out at first mention.

E-mail Your Manuscript to: jdpa@dermpa.org

Note: Hard copies are not accepted

JDPA MANUSCRIPT PREPARATION CHECKLIST

✓ **TITLE PAGE**

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Word Count. List main body word count (Do not include references and supplementary material).
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Keywords. Include any search terms relevant to the manuscript content.
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✓ **FIGURES, TABLES, & SUPPLEMENTAL MATERIAL**

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Supplemental Material. References to any online supplemental information must appear in the main article. Such supplemental information can include but are not limited to additional tables, figures, videos, audio files, slide shows, data sets (including qualitative data), and online appendices. If your study is based on a survey, consider submitting your survey instrument or the key questions as a data supplement. Authors are responsible for clearly labeling supplemental information and are accountable for its accuracy. Supplemental information will be peer reviewed, but not professionally copyedited.

Bringing Molluscum Contagiosum to Light

Cross-section of skin infected with molluscum contagiosum

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While as many as 1 out of every 5 healthy children contract molluscum contagiosum, this disease and the patients it affects receive very little attention.[1] Quality of life can be negatively affected by a molluscum infection.[2] Children with the disease may become stigmatized and experience teasing, embarrassment, and social isolation. Up to 82% of parents and caregivers express moderate to great concern about molluscum.[3] Lesions may be mostly asymptomatic, but reports indicate that patients do complain about itching, burning, and tenderness.[3]

Although lesions can resolve within 6 to 9 months, patients typically have the infection for 13 months, and some infections can persist for 2 years or more.[2,3] Treatment at the time of diagnosis provides the best chance of decreasing the number of lesions and spread of the disease.[3]

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Our proprietary drug-device combination is currently being evaluated in patients with molluscum contagiosum in two Phase 3 trials.

References

1. Berger EM, et al. *Arch Dermatol*. 2012;148(11):1257-64. **2.** Hsu J and Tom W. *Practical Dermatology for Pediatrics*. 2010:34-37. **3.** Shisler JL. Chapter Four - Immune Evasion Strategies of Molluscum Contagiosum Virus. In: Maramorosch K, Mettenleiter TN. eds. *Advances in Virus Research*. Cambridge, MA; Academic Press; 2015.

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Important Revisions to Dermatology Reflected in Updated American Academy for Physician Assistants' Sample Core and Specialty Privileges for PAs

As part of a collection practice resources for physician assistants (PAs), the American Academy of Physician Assistants (AAPA) provides a guide for regulators, hospitals, employers, and third-party payers on credentialing, privileging, and assessing clinical competency of PAs as part of a larger effort to better define the training, competencies, and the scope of practice of PAs. Such guides are described by AAPA as a "win" for PAs, employers, and patients because knowledge of PA practice can optimize patient care while maintaining compliance with Federal laws and regulations.

Updated in August 2020 with the input of clinicians in multiple areas of practice, the Sample Core and Specialty Privileges for PAs breaks down a wide variety of competencies commonly expected in clinical practice. With the assistance of Laura Bush, DMSc, PA-C, DFAAPA, and Hannah Rodriguez, MPAS, PA-C, Directors-at-Large of the Society of Dermatology for Physician Assistants (SDPA), important recommendations were proposed and implemented, bringing the number of privileges for PAs in dermatology from 6 to 24. Defined in the new document, additional dermatology privileges include tasks such as interpreting pathology reports, serving as first assist in surgery, including Mohs, and performing an array of clinical and aesthetic procedures (e.g., laser, photodynamic therapy, microscopy).

PREVIOUS LISTING:
Dermatology Privileges for PAs

- Chemical peels
- Cryosurgery
- Inject botulinum, fillers, and cosmetic agents
- Electrodessication and curettage
- Microdermabrasion
- Perform punch and excisional biopsies

NEW LISTING:
Dermatology Privileges for PAs

- Apply Unna boot
- Apply and manage negative pressure therapy (i.e. wound vacuum)
- Chemical peels
- Cryosurgery
- Dermoscopy
- Inject botulinum, fillers, and cosmetic agents
- Injection sclerotherapy
- Interpret pathology reports
- Electrodessication and curettage
- Microdermabrasion
- Perform bacterial/viral/fungal cultures
- Perform body contouring and tightening procedures
- Perform intralesional injections
- Perform laser procedures
- Perform microneedling
- Perform microscopy
- Perform narrow band UVB phototherapy
- Perform patch testing
- Perform photodynamic therapy
- Perform superficial radiation therapy
- Perform Wood's lamp evaluation
- Surgical first assist; including Moh's Surgery
- Surgical site marking
- Wound care and debridement

For the complete updated document as well as other guides, visit the AAPA's PA Practice Resource Center at https://www.aapa.org/career-central/practice-tools/pa-practice-resources/

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SDPA Presents 2020 Digital Abstracts
CONTENTS

Exploratory Study of the Association Between Spironolactone Use for the Treatment of Acne Vulgaris and Premenstrual Syndrome Symptom Improvement in Female Patients

Taylor Bach, PA-C, Rachel Dorrer, PA-C, Nicole DeMott, PA-C, Megan Dauscher PA-C, Christina Ventura DrPH

Professional Affiliations: Hofstra University PA Program

Introduction: Premenstrual syndrome (PMS) is commonly experienced by women of reproductive age, and reduces the quality of life of those who experience it severely. Research on options for women who may not want to be on hormonal contraceptives to treat PMS symptoms are limited, although spironolactone presents a viable choice for women with hormonal acne.

Methods: A quantitative survey was disseminated to patients currently being treated with spironolactone at a dermatology practice on Long Island, NY via anonymous QR codes during patient encounters. Questions captured details related to spironolactone treatment as well as demographics, PMS symptom experience before and during treatment, and self-reported quality of life and self-esteem measures.

Results: A total of N=56 female participants responded to the survey, with an average age of 30.6 years old. While patients reported an overwhelmingly positive experience of being on the medication, as well as an improvement in their self-confidence and self-esteem being on spironolactone therapy, there was not a statistically significant association between improvement of PMS symptoms based on dosage and duration of therapy (p=0.726 and p=0.557, respectively).

Conclusions: Although spironolactone has been shown in some studies to improve PMS symptomology, it was not associated with an improvement in this study. Improved patient communication and interprofessional collaboration between dermatologists and gynecologists may help to better educate patients and improve their understanding of their comprehensive symptomology and subsequent symptom resolution.

Efficacy of Tapinarof Cream by Body Region in Subjects with Plaque Psoriasis in a Phase 2b Randomized Controlled Study

Robert Bissonnette,[1] Linda Stein Gold,[2] Leon Kircik,[3,4] Stephen Tyring,[5] Anna M. Tallman,[6] April Armstrong[7]

[1]Innovaderm Research Inc, Montreal, QC, Canada, [2]Henry Ford Health System, Detroit, MI, USA, [3]Skin Sciences PLLC, Louisville, KY, USA, [4]Icahn School of Medicine at Mount Sinai, NY, USA, [5]University of Texas Health Science Center, Houston, TX, USA, [6]Dermavant Sciences, Inc., Long Beach, CA, USA, [7]Keck School of Medicine at University of Southern California, Los Angeles, CA, USA

Tapinarof is a therapeutic aryl hydrocarbon receptor modulating agent (TAMA) in development for treatment of psoriasis and atopic dermatitis. In a phase 2b study, Physician Global Assessment (PGA) and Psoriasis Area and Severity Index (PASI) responses at Week 12 were significantly higher in all tapinarof groups vs vehicle. Higher responses in tapinarof groups were maintained for 4 weeks post-treatment vs vehicle.[1] This *post-hoc* analysis evaluated mean change in PASI from baseline by body region.

Of 227 subjects randomized, 175 completed the study. Overall mean baseline PASI score was 8.8 and most subjects (80%) had a PGA score of 3 (moderate). Mean PASI improvements at Week 12 were significantly greater in tapinarof 1% twice-daily (BID), 1% once-daily (QD), 0.5% BID, and 0.5% QD groups vs vehicle BID and QD, overall: –8.70, –6.62, –6.30, and –5.41 vs –2.77 and –1.54, respectively (all P<0.001); in the upper extremities: –9.65, –9.05, –8.70, and –6.04 vs –4.88 and –1.61 (all P<0.05); and lower extremities: –8.74, –8.19, –7.16, and –6.33 vs –2.47 and –2.0 (all P<0.001). In the trunk and head/neck, PASI improvements were significantly greater in all tapinarof groups vs vehicle except the 0.5% BID group: –11.94, –9.13, –9.0, and –8.25 vs –4.08 and –1.85 (P<0.01); and –9.0, –7.40, –5.0, and –9.0 vs –1.75 and –2.50 (P<0.05), respectively.

Tapinarof cream was generally well tolerated; most adverse events were mild or moderate.

Tapinarof cream demonstrated consistent efficacy across body regions as measured by PASI and was generally well tolerated. Two phase 3 studies of tapinarof cream 1% QD in psoriasis are ongoing: PSOARING 1 (NCT03956355) and PSOARING 2 (NCT03983980).

Reference: 1. Robbins K et al. *J Am Acad Dermatol*. 2019;80:714–721.

Tapinarof Cream for the Treatment of Plaque Psoriasis: Efficacy And Safety by Baseline Disease Characteristics and Skin Type in a Phase 2B Randomized Study

Mark Lebwohl,[1] James Del Rosso,[2] Chih-ho Hong,[3] Anna Tallman,[4] Leon Kircik1,[5]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV, USA; [3]University of British Columbia and Probity Medical Research, Surrey, BC, Canada; [4]Dermavant Sciences, Inc., New York, NY, USA; [5]Skin Sciences, PLLC, Louisville, KY, USA

Tapinarof is a therapeutic aryl hydrocarbon receptor modulating agent (TAMA) in development for the treatment of psoriasis and atopic dermatitis. In a previously reported phase 2b efficacy and safety study (NCT02564042), Physician Global Assessment (PGA) responses (0 or 1 and ≥2-grade improvement from baseline) at Week 12 were significantly higher in all tapinarof cream groups vs vehicle. Tapinarof cream demonstrated durable PGA responses through 4 weeks after the end of study treatment.[1]

A post-hoc analysis of PGA response stratified by baseline % body surface area (BSA) affected, psoriasis duration, and Fitzpatrick skin type was conducted to evaluate the efficacy and safety of tapinarof cream vs vehicle across subgroups.

Overall, mean baseline disease characteristics were comparable across groups. Most subjects (80%) had a baseline PGA score of 3 (moderate). Mean baseline Psoriasis Area and Severity Index score was 8.8. Stratified by baseline BSA, PGA response at Week 12 in subjects treated with tapinarof 1% twice daily (BID), 1% once daily (QD), 0.5% BID, and 0.5% QD vs vehicle BID and

vehicle QD was: 67%, 60%, 33%, and 35% vs 13% and 6%, respectively (1 to <10% BSA affected; n=102); and 64%, 40%, 75%, and 38% vs 0% and 0%, respectively (≥10% BSA affected; n=39). Stratified by psoriasis duration, PGA response at Week 12 in subjects treated with tapinarof 1% BID, 1% QD, 0.5% BID, and 0.5% QD vs vehicle BID and vehicle QD was: 50%, 80%, 50%, and 29% vs 0% and 0%, respectively (6 months to <5 years; n=27); 67%, 50%, 20%, and 50% vs 25% and 0% (5 years to <10 years; n=32); and 73%, 50%, 53%, and 33% vs 8% and 8% (≥10 years; n=82). Stratified by Fitzpatrick skin type, PGA response at Week 12 in subjects treated with tapinarof 1% BID, 1% QD, 0.5% BID, and 0.5% QD vs vehicle BID and vehicle QD was: 60%, 67%, 50%, and 25% vs 0% and 10%, respectively (Fitzpatrick skin type I/II; n=41); 54%, 47%, 60%, and 44% vs 18% and 0% (Fitzpatrick skin type III/IV; n=73); and 100%, 75%, 25%, and 25% vs 0% and 0% (Fitzpatrick skin type V/VI; n=27). Incidence and type of adverse events were generally comparable across groups and consistent with those observed in the overall population.

Tapinarof cream was efficacious and well tolerated across subgroups regardless of baseline % BSA affected, psoriasis duration, or Fitzpatrick skin type. Two phase 3 studies of tapinarof cream 1% QD in psoriasis are ongoing: PSOARING 1 (NCT03956355) and PSOARING 2 (NCT03983980).

Reference: 1. Robbins K et al. *J Am Acad Dermatol.* 2019;80:714–721.

Absolute PASI Response Up to 52 Weeks with Brodalumab in Patients with Moderate-to-Severe Plaque Psoriasis

Matthew Brunner,[1] April Armstrong,[2] Bruce Strober,[3,4] Benjamin Ehst,[5] Abby Jacobson,[6] Uduak Ntuen[6]

1The Dermatology & Skin Surgery Center, Stockbridge, GA; 2University of Southern California, Los Angeles, CA; 3Yale University, New Haven, CT; 4Central Connecticut Dermatology, Cromwell, CT; 5Oregon Medical Research Center, Portland, OR; 6Ortho Dermatologics (a division of Bausch Health US, LLC), Bridgewater, NJ

Introduction: Skin clearance measured by absolute psoriasis area and severity index (PASI) may provide more clinically relevant information on disease severity than relative PASI improvement.[1,2] Brodalumab is a fully human anti–interleukin-17 receptor A monoclonal antibody efficacious for the treatment of adults with moderate-to-severe psoriasis.[3] In this post hoc analysis, absolute PASI was evaluated through 52 weeks of treatment with brodalumab in a randomized phase 3 trial (AMAGINE-1). The purpose of the study was to evaluate the efficacy of brodalumab compared with placebo as measured by absolute PASI in patients with moderate-to-severe plaque psoriasis after 12 weeks of treatment and to assess the efficacy of brodalumab measured by absolute PASI through 52 weeks in patients with moderate-to-severe plaque psoriasis.

Methods: Patients were initially randomized to brodalumab 210 mg every 2 weeks (Q2W) or placebo in a 12-week induction phase. After 12 weeks, a subset of patients with a robust response continued to receive brodalumab 210 mg Q2W through 52 weeks. Skin clearance was assessed as absolute PASI from baseline up to 52 weeks. Efficacy data were reported using multiple imputation (induction phase) and last observation carried forward (rerandomization phase) analyses.

Results: In the induction phase, patients received brodalumab 210 mg Q2W (n=222) or placebo (n=220). Baseline mean absolute PASI was similar between groups (brodalumab: 19.41; placebo: 19.72). At week 12, mean (standard error) absolute PASI was significantly lower in patients who received brodalumab (2.75 [0.39]) than that in patients receiving placebo (20.01 [0.72]; least squares mean treatment difference vs placebo, –17.21; P<0.001). Following rerandomization at week 12, 83 patients remained on brodalumab 210 mg Q2W. Mean (standard deviation) absolute PASI in these patients was 0.77 (2.08) at week 52.

Conclusions: Treatment with continuous brodalumab over 52 weeks resulted in significantly decreased absolute PASI in patients with moderate-to-severe plaque psoriasis.

References:

1. Takeshita et al. *J Am Acad Dermatol.* 2014;71(4):633-641. 2. Petto et al. *J Am Acad Dermatol.* 2016;74(5):AB234. 3. Papp et al. *Br J Dermatol.* 2016;175:273-286.

Funding: This study was sponsored by Ortho Dermatologics (a division of Bausch Health US, LLC). Medical writing support was provided by MedThink SciCom under the direction of the authors and was funded by Ortho Dermatologics.

Encore: Data from this abstract were previously presented in full at the 78th Annual Meeting of the American Academy of Dermatology; March 20-24, 2020; Denver, CO. Poster 15921.

Importance of Complete Skin Clearance on Quality of Life: Analysis of Three Phase 3 Studies

Archana Miriam Sangha,[1] April Armstrong,[2] Andrew Blauvelt,[3] Scott Drew,[4] Roger Ho,[5] Abby Jacobson[6]

[1]Anne Arundel Dermatology, Vienna, VA; [2]University of Southern California, Los Angeles, CA; [3]Oregon Medical Research Center, Portland, OR; [4]OhioHealth, Marion, OH; [5]The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, NY; [6]Ortho Dermatologics (a division of Bausch Health US, LLC), Bridgewater, NJ

Introduction: Complete skin clearance is an important treatment goal for patients with psoriasis. Evidence shows that complete skin clearance is associated with several benefits over almost-clear skin, including improved quality of life. In the phase 3 brodalumab trials AMAGINE-1, -2, and -3, 42%, 44%, and 37% of patients receiving brodalumab 210 mg every 2 weeks (Q2W), respectively, achieved a Psoriasis Area and Severity Index score of 100 (PASI 100) at week 12. The purpose of this analysis was to explore whether patients with psoriasis achieving complete skin clearance experienced greater improvements in quality of life than those achieving a good but less than complete response.

Methods: Data for this post hoc analysis were pooled from the 12-week induction phases of three phase 3 clinical trials (AMAGINE-1/-2/-3). Patients included in the analysis were treated with brodalumab (140 or 210 mg) or ustekinumab (45 or 90 mg) and had achieved complete skin clearance, defined as 100% improvement in PASI score (PASI 100), or good but incomplete skin clearance, defined as PASI 90 to <100. Quality of life was assessed using mental and physical component scores (MCS and PCS) of the Short Form 36 (SF-36) health survey, the Hospital Anxiety and Depression Scale (HADS), and the Work Limitations Questionnaire (WLQ).

Results: At week 12, mean (standard deviation [SD]) HADS anxiety and depression scores were numerically lower for patients achieving PASI 100 (anxiety, 4.75 [3.30]; depression, 2.90 [3.00]) than for patients achieving PASI 90 to <100 (anxiety, 5.09 [4.16]; depression, 3.55 [3.18]). Numerically fewer work limitations, indicated by mean (SD) WLQ scores, were reported by patients achieving PASI 100 (2.29 [3.11]) than by those achieving PASI 90 to <100 (3.00 [3.58]). At week 12, mean (SD) SF-36 MCS and PCS were similar among patients who achieved PASI 90 to <100 (MCS, 51.39 [7.68]; PCS, 52.53 [7.82]) and PASI 100 (MCS, 52.96 [7.99]; PCS, 52.38 [8.71]).

Conclusions: Achievement of complete skin clearance (PASI 100) was associated with greater numeric improvements in quality-of-life measures than achievement of a good but less than complete response in patients with moderate-to-severe plaque psoriasis. These results suggest that therapies likely to help patients achieve complete skin clearance, such as brodalumab, are important to consider when making treatment decisions.

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A Multi-Center, Open-Label Extension Study to Assess the Long-term Safety/Tolerability and Pharmacokinetics, and Explore the Efficacy of Sofpironium Bromide Gel, 15% Applied Topically to Children and Adolescents, 9to 16 Years of Age, with Primary Axillary Hyperhidrosis

Brandon Kirsch, MD[1], Janet DuBois, MD[2], Martin N. Zaiac, MD[3], Sanjeev Ahuja, MD, MBA, FACP[4], Deepak Chadha, MS, MBA, RAC[5]

[1]Kirsch Dermatology, Naples, FL, [2]DermResearch Inc., Austin, TX, [3]Sweet Hope Research Specialty, Hialeah, FL, [4]Former CMO, Brickell Biotech, Inc., Boulder, CO, [5]Brickell Biotech, Inc., Boulder, CO

Introduction: ~2.1% of the US population aged <18 years has primary hyperhidrosis (HH); ~65% have axillary HH. Long-term safety/tolerability and efficacy of topical HH treatments have rarely been studied in pediatric patients. Sofpironium bromide is a retrometabolically designed analog of glycopyrrolate (anticholinergic) in development for topical treatment of primary axillary HH. Absorbed drug is rapidly metabolized, potentially allowing optimal local therapeutic effect with minimal systemic effects.

Procedures: 21 of 25 subjects (age 9-16 yrs) with primary axillary HH of ≥6 months duration, completing a previous 1-week safety and pharmacokinetic (PK) study (BBI- 4000-CL-105), were enrolled. Objectives were to assess safety/tolerability and PK, and explore efficacy of sofpironium bromide gel, 15% applied to both axillae for 24 weeks.

Results: Mean age (SD) 13.3 (2.29) years. 16 subjects completed this 24-week study. 7 had treatment emergent adverse events (TEAEs); 4 with AEs related to study drug, including expected systemic anticholinergic AEs (blurred vision, dry mouth, dry eyes, mydriasis) and local events (pain, pruritus, rash, erythema). 2 subjects discontinued due to TEAEs, including dry eye, dry mouth, local pruritus, local rash. PK did not show evidence of drug/major metabolite accumulation, with most subjects having concentrations not quantifiable. The validated patient-reported outcome, Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax), showed mean (SD) change from baseline (from previous study) to Week 24 of this study of -1.91 (1.038). A -1.00 change shows clinically meaningful improvement.

Conclusion: In this 24-week study in pediatric subjects sofpironium bromide, 15% was safe/well tolerated. Majority of subjects had no TEAE, and there were no severe or serious AEs. There was no evidence of drug accumulation. There was indication of clinically meaningful improvement in axillary HH.

The study was funded by Brickell Biotech, Inc.

Use of Topical Corticosteroids Plus Tralokinumab in Adult Patients with Moderate-to-Severe Atopic Dermatitis: Results from the 32-Week, Phase 3 Ecztra 3 Trial

Jonathan I. Silverberg,[1] Andrew E. Pink,[2] Azra Kurbasic,[3] Christina Kurre Olsen,[3] Stephan Weidinger[4]

[1]Department of Dermatology, The George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [2]St. John's Institute of Dermatology, Guy's and St. Thomas' Hospitals, London, UK; [3]LEO Pharma A/S, Ballerup, Denmark; [4]Department of Dermatology and Allergy, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

Introduction: Although topical corticosteroids (TCS) are mainstay of treatment for patients with atopic dermatitis (AD), they are often insufficient to achieve disease control, and their use is limited by safety concerns and poor adherence. Tralokinumab is a fully human monoclonal antibody that specifically neutralizes interleukin-13, a key type 2 cytokine involved in the pathogenesis of AD. The objective of this study was to assess the efficacy, safety, and use of combination treatment with tralokinumab + TCS in patients to moderate-to-severe AD.

Methods: In this double-blind, randomized, 32-week clinical trial (NCT03363854), patients with moderate-

to-severe AD were randomized 2:1 to subcutaneous tralokinumab 300 mg or placebo every 2 weeks (Q2W) + TCS (mometasone furoate 0.1% cream), which was allowed once daily as needed on lesional skin from randomization to the end of the trial. Lower-potency TCS or topical calcineurin inhibitors (TCI) could be used on areas where use of the supplied TCS was not advisable. Rescue treatment in the form of topical and/or systemic medications was permitted to control intolerable AD symptoms. Primary endpoints were Investigator's Global Assessment (IGA)-0/1 and Eczema Area and Severity Index (EASI)-75 at week 16. Secondary endpoints included the amount of TCS used. At week 16, responders to tralokinumab (IGA-0/1 and/or EASI-75) were re-randomized 1:1 to tralokinumab Q2W or Q4W + TCS for an additional 16 weeks. Placebo responders continued placebo Q2W + TCS; all nonresponders received tralokinumab Q2W + TCS.

Results: At week 16, the proportion of patients achieving IGA-0/1 (38.9% vs 26.2%; p=0.015) and EASI-75 (56.0% vs 35.7%; p<0.001) was significantly higher in the tralokinumab+TCS than in the placebo+TCS group. A smaller proportion of patients treated with tralokinumab than those who received placebo used rescue treatment through week 16 (2.8% vs 10.2%). Less TCS was used cumulatively by patients treated with tralokinumab than those who received placebo through week 16 (134.9 g vs 193.5 g; Δ –58.6). The majority of week-16 tralokinumab responders maintained response at week 32 with tralokinumab, irrespective of dosing frequency. The overall incidence of adverse events was similar across treatment groups and did not increase with prolonged treatment.

Conclusions: Tralokinumab 300 mg Q2W + TCS was significantly more effective than placebo Q2W + TCS in treating patients with moderate-to-severe AD. TCS use was lower with tralokinumab than placebo, demonstrating the potential steroid-sparing effects of tralokinumab.

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Tralokinumab Improves Clinically Relevant Outcome Measures: a Post Hoc Analysis of Ecztra 3, a Randomized Clinical Trial in Patients with Moderate-to-Severe Atopic Dermatitis

Stephan Weidinger,[1] Andrew E. Pink, [2]Juan Francisco Silvestre, [3]Azra Kurbasic, [4]Christina Kurre Olsen, [4]Andreas Westh Vilsbøll, [4]Marjolein de Bruin Weller[5]

[1]Department of Dermatology and Allergy, University Hospital Schleswig-Holstein, Kiel, Germany; [2]St John's Institute of Dermatology, Guy's and St. Thomas' Hospitals, London, UK; [3]Dermatology Department, Hospital General Universitario de Alicante, Alicante, Spain; [4]LEO Pharma A/S, Ballerup, Denmark; [5]Department of Allergology and Dermatology, University Medical Centre Utrecht, National Expertise Center for Eczema, Utrecht, the Netherlands

Introduction: Investigator's Global Assessment 0 or 1 (IGA-0/1; clear or almost clear skin) and ≥75% improvement in Eczema Area and Severity Index (EASI-75) are the regulatory primary efficacy endpoints in Phase 3 trials of atopic dermatitis (AD). These endpoints, however, may not reflect the full burden of AD and may not provide sufficient information for clinical decision making. This objective of this study was to assess the response to treatment with tralokinumab in combination with topical corticosteroids (TCS) based on targets and time points typically used in clinical practice.

Methods: In the ECZTRA 3 trial (NCT03363854), adult patients with moderate-to-severe AD were randomized 2:1 to subcutaneous tralokinumab 300 mg every 2 weeks (Q2W) or placebo Q2W for 16 weeks. Patients in both groups used concomitant TCS as needed. At week 16, tralokinumab responders (IGA-0/1 and/or EASI-75) were re-randomized 1:1 to tralokinumab Q2W or Q4W+TCS, whereas nonresponders were treated with tralokinumab Q2W+TCS for an additional 16 weeks. This post hoc analysis assessed the proportion of patients achieving clinically meaningful response after 12 and 24 weeks based on clinician-assessed signs (EASI), patient-reported symptoms (pruritus and Patient-Oriented Eczema Measure [POEM]), and patient-reported quality of life (Dermatology Life Quality Index [DLQI] and Patient Global Impression of Bother [PGI-B]). Chosen time points reflect typical follow-up for adult AD patients initiating new treatment.

Results: During the initial 16-week treatment period, 252 and 126 patients received tralokinumab Q2W+TCS and placebo Q2W+TCS, respectively. At week 16, significantly more patients treated with tralokinumab+TCS than those who received placebo+TCS achieved the regulatory primary endpoints of IGA-0/1 (38.9%, p=0.015) and EASI-75 (56.0%, p<0.001). At week 12, 79.0% of the 252 patients who received tralokinumab+TCS achieved EASI-50, 59.0% achieved ≥3-point reduction in worst daily pruritus, 78.0% achieved ≥4-point reduction in POEM, 77.0% achieved ≥4 point reduction in DLQI, and 80.2%, achieved ≥1-point reduction in PGI-B. A high proportion (79.4%; 196/247 assessed) achieved both ≥1-point reduction in PGI-B and at least one of the other disease domain endpoints. At week 24, 81.0% (N=252) achieved EASI-50, and 69.0% achieved EASI-75, while week-24 response rates in the subgroup with both the PGI-B target and any of the other disease domains at week 12 (N=196) were 90.8% and 75.5% for EASI-50 and EASI-75, respectively.

Conclusions: Tralokinumab in combination with TCS was associated with a high proportion of patients achieving

and maintaining clinically meaningful improvements in AD signs and symptoms and AD-related quality of life after 12 and 24 weeks of treatment.

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Laboratory Safety of Dupilumab in Pediatric Patients Aged ≥6 to <12 Years With Severe Atopic Dermatitis: Results From a Phase 3 Trial (LIBERTY AD PEDS)

Andreas Wollenberg[1], Diamant Thaçi[2], Michael J. Cork[3], Peter D. Arkwright[4], Melinda Gooderham[5], Xian Sun[6], John T. O'Malley[7], Faisal A. Khokhar[6], Ashish Bansal[6], Brad Shumel[6]

[1]Ludwig-Maximilian University, Munich, Germany; [2]University of Lübeck, Lubeck, Germany; [3]University of Sheffield, Sheffield, UK; [4]University of Manchester, Manchester, UK; [5]SKiN Centre for Dermatology, and Queen's University, Kingston, ON, Canada; [6]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [7]Sanofi, Cambridge, MA, USA

Introduction: Most current systemic treatments for moderate-to-severe atopic dermatitis (AD) require serial laboratory assessments to ensure patient safety. Dupilumab has demonstrated significant clinical improvement with a favorable risk–benefit profile in adults and adolescents with moderate-to-severe AD inadequately controlled with topical medications and in children aged ≥6 to <12 years with severe AD. Moreover, no clinically important changes in hematology, serum chemistry, and urinalysis parameters have been reported for dupilumab-treated adults and adolescents. The impact of dupilumab treatment on laboratory values in children aged ≥6 to <12 years with severe AD is not known.

Methods: In LIBERTY AD PEDS (NCT03345914), a multicenter, phase 3 trial, 367 patients aged ≥6 to <12 years were randomized 1:1:1 to subcutaneous dupilumab every 2 weeks (q2w; 100 mg if baseline weight <30 kg, 200 mg if ≥30 kg) or every 4 weeks (q4w; 300 mg), or placebo for 16 weeks. All patients received concomitant medium-potency topical corticosteroids. Laboratory values for hematology parameters and serum chemistry were assessed at baseline and Weeks 4, 8, and 16.

Results: Safety was assessed in 362 patients (q2w/q4w/placebo: n=122/n=120/n=120). At baseline, treatment groups had similar demographic, clinical, and laboratory characteristics. Baseline mean eosinophil counts were 0.82/0.83/0.85 (x109/L) for q2w/q4w/placebo. Increases from baseline in mean eosinophil counts (x109/L) were observed in all groups, with the highest mean increase at Week 8 for placebo (+0.10) and dupilumab q4w (+0.17), and at Week 16 for dupilumab q2w (+0.25). No clinically treatment-related relevant events were associated with eosinophilia. There were no meaningful trends in mean changes from baseline in leukocyte counts (x109/L; q2w −0.10; q4w −0.19; placebo −0.14) or hemoglobin levels (g/L; q2w −1.5; q4w −1.6; placebo +0.4) at Week 16. Mean platelet values were lower in both dupilumab groups compared to baseline at Weeks 4/8/16 (x109/L, q2w −19.3; q4w −18.8; placebo +5.0 at Week 16), but remained within normal range. There were no clinically meaningful trends in mean changes from baseline in chemistry parameters in any group. Mean decreases from baseline in lactate dehydrogenase (LDH) were observed in both dupilumab groups up to Week 16 (U/L, q2w −42.2; q4w −39.4; placebo −0.4 at Week 16).

Conclusions: There were no clinically important changes in laboratory parameters attributable to dupilumab treatment in children aged ≥6 to <12 years with severe AD in LIBERTY AD PEDS. Consistent with a reduction in systemic inflammation, decreases in platelet counts and LDH levels – both considered acute-phase reactants – were observed in both the dupilumab q2w and q4w groups.

Dupilumab Prevents Flares in Adults with Moderate-to-Severe Atopic Dermatitis in a 52-Week, Randomized, Controlled, Phase 3 Trial

J.F. Merola[1], R. Sidbury[2], A. Wollenberg[3], Z. Chen[4], A. Zhang[5], B. Shumel[4], A. Abramova[4], A.B. Rossi[5]

[1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [2]Seattle Children's Hospital, Seattle, WA, USA; [3]Ludwig-Maximilian University, Munich, Germany; [4]Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; [5]Sanofi Genzyme, Cambridge MA, USA

Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by flares, defined as worsening of the disease requiring escalation or intensification of AD treatment. Flare prevention is a hallmark of long-term disease control in AD. Here, we report the effect of dupilumab treatment for 52 weeks on flare prevention in adults with moderate-to-severe AD from the LIBERTY AD CHRONOS trial (NCT02260986).

Methods: In this trial, 740 patients (pts) with moderate-to-severe AD were randomized 3:1:3 to subcutaneous dupilumab 300 mg once weekly, dupilumab 300 mg every 2 weeks (q2w), or placebo (PBO); all pts also received a standardized regimen of medium-potency topical corticosteroids (TCS). This analysis includes pts who received the approved dupilumab q2w+TCS dose or PBO+TCS for 52 weeks.

Results: During the 52-week treatment period, the annualized flare rate (AFR) was significantly higher in pts who received PBO+TCS (AFR = 0.77, 95% confidence interval [CI] 0.63–0.93) than in those who received dupilumab q2w+TCS (AFR = 0.17, 95% CI 0.10–0.29),

representing a 78% relative reduction in annual flares in pts who were treated with dupilumab q2w+TCS (relative risk = 0.22, 95% CI 0.13–0.39). P values for all comparisons on event rate between dupilumab q2w and PBO were < 0.05 based on a parametric Poisson model. In the 12 months before enrollment, 89/106 (84%) and 243/315 (77%) pts receiving dupilumab q2w+TCS and PBO+TCS, respectively, self-reported AD flares. During the 52-week treatment period, only 14% of pts receiving dupilumab q2w+TCS experienced a flare vs 43% of pts receiving PBO+TCS.

Conclusion: These results demonstrate that dupilumab prevents flares in adults with moderate-to-severe AD, providing continuous, long-term disease control.

Long-Term Treatment with Dupilumab Minimizes Use of Systemic Immunosuppressants as Rescue Medications in Adults with Moderate-to-Severe Atopic Dermatitis

L.A. Beck[1], A. Blauvelt[2], L. Sher[3], I. Hussain[4], A.B. Rossi[5], Z. Chen[6], B. Shumel[6], S. Bansal[6]

[1]University of Rochester Medical Center, Rochester, NY; [2]Oregon Medical Research Center, Portland, OR; [3]Peninsula Research Associates, Rolling Hills Estate, CA; [4]Vital Prospects Clinical Research Institute, PC, Tulsa, OK; [5]Sanofi Genzyme, Cambridge, MA; [6]Regeneron Pharmaceuticals, Inc., Tarrytown, NY; USA

Background: LIBERTY AD OLE (NCT01949311) is a phase 3, open-label extension study that evaluates the long-term safety and efficacy of dupilumab in adults with moderate-to-severe atopic dermatitis (AD) who were previously enrolled in dupilumab clinical trials. Here, we report the proportion of patients (pts) who required systemic rescue medications.

Methods: All pts who received ≥ 1 dose of dupilumab and required ≥ 1 concomitant rescue medication during the study were included in this analysis. Rescue treatments included systemic corticosteroids, nonsteroidal systemic immunosuppressants (ISS), and phototherapy, administered at the investigator's discretion to treat intolerable AD symptoms or to manage serious intercurrent conditions.

Results: At the data cutoff date, 2,677 pts received dupilumab for up to 148 weeks. Most patients (82.4%) had completed the study through the Week 52 visit, and 13% had completed up to the Week 148 visit. Previous use of nonsteroidal systemic ISS for AD was reported in 39.3% (1,051 pts); 34.2% (915 pts) previously received cyclosporine, 10.6% (284 pts) methotrexate, and 6.4% (172 pts) azathioprine. During the OLE study, systemic rescue medications were required in 7.5% (200 pts); the majority (93.5% [187 pts]) received systemic corticosteroids, and 10.5% (21 pts) received systemic nonsteroidal ISS.

Conclusion: Dupilumab treatment markedly reduced the need for systemic ISS therapies in adults with moderate-to-severe AD. The long-term safety profile of dupilumab remained consistent with the safety profile previously observed in controlled studies in adults with moderate-to-severe AD.

Secukinumab Is Highly Efficacious and Has a Favorable Safety Profile in Pediatric Patients with Moderate-to-Severe Plaque Psoriasis

Nina Magnolo, MD,[1] Külli Kingo, MD, PhD,[2] Vivian Laquer, MD,[3] John Browning, MD,[4] Deborah Keefe, MD,[5] Rafal Mazur, MD,[6] Prayashi Ghelani, BSc, MSc,[7] Manmath Patekar, MD,[6] LindaAnn Wraith, MBA,[5] Adam Reich, MD, PhD[8]

[1]University Hospital Münster, Münster, Germany; [2]Tartu University Hospital and University of Tartu, Tartu, Estonia; [3]First OC Dermatology, Fountain Valley, CA; [4]University of Texas San Antonio, San Antonio, TX; [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ; [6]Novartis Pharma AG, Basel, Switzerland; [7]264957 Ontario Limited, Ontario, Canada; [8]University of Rzeszów, Rzeszów, Poland

Background: Psoriasis affects approximately 1% of children and adolescents; few treatment options are available, resulting in a high unmet medical need. This study investigated the efficacy and safety of 2 secukinumab dosing regimens in pediatric patients with moderate-to-severe plaque psoriasis.

Methods: In this ongoing, randomized, multicenter, open-label study (NCT03668613), patients aged 6 to <18 years with moderate-to-severe plaque psoriasis were stratified by weight and randomized 1:1 to receive low-dose (LD; 75-150 mg; n = 42) or high-dose (HD; 75-300 mg; n = 42) subcutaneous secukinumab. Efficacy was determined at week 12 according to PASI75/90/100 and IGA mod 2011 0/1 responses (nonresponder imputation); quality of life (QOL) was determined using Children's DLQI (CDLQI) 0/1 responses. Safety was evaluated through week 16 by the incidence of treatment-emergent adverse events (TEAEs).

Results: Predictive log odds ratios from a Bayesian analysis for PASI75, PASI90, and IGA 0/1 responses at week 12 suggest benefit over historical placebo for both regimens (probability of [log-OR > 0] = 1). At week 12, achievement of responses was similar in both arms (PASI75/90/100: LD, 92.9%/69.0%/59.5%; HD, 92.9%/76.2%/54.8% and IGA 0/1: LD, 78.6%; HD, 81.0%). Patients in both arms experienced improved QOL at week 12 as measured by CDLQI 0/1 responses (LD, 50.0%; HD, 61.9%). TEAEs were comparable between treatment arms and consistent with the known safety profile of secukinumab.

Conclusion: Across both doses, secukinumab is highly efficacious in rapidly improving skin symptoms and QOL in pediatric patients with moderate-to-severe plaque psoriasis and has a favorable safety profile.

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Efficacy and Safety of Bimekizumab in Patients with Moderate to Severe Plaque Psoriasis: Results from BE READY, a 56-Week Phase 3, Randomized, Double-Blinded, Placebo-Controlled Study with Randomized Withdrawal

Kenneth Gordon,[1] Peter Foley,[2] James Krueger,[3] Andreas Pinter,[4] Kristian Reich,[5] Ronald Vender,[6] Veerle Vanvoorden,[7] Cynthia Madden,[8] Luke Peterson,[8] Andrew Blauvelt[9]

[1]Medical College of Wisconsin, Milwaukee, WI, USA; [2]Skin Health Institute, Carlton, Victoria, Australia; [3]The Rockefeller University, New York, NY, USA; [4]University Hospital Frankfurt am Main, Department of Dermatology, Frankfurt am Main, Germany; [5]Center for Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf and Skinflammation® Center, Hamburg, Germany; [6]Division of Dermatology, McMaster University, Hamilton, Ontario, Canada; [7]UCB Pharma, Brussels, Belgium; [8]UCB Pharma, Raleigh, NC, USA; [9]Oregon Medical Research Center, Portland, OR, USA

Introduction: Increasing evidence indicates that interleukin (IL)-17A and IL-17F contribute to the immunopathogenesis of psoriasis, a mainly Th17-driven disease.[1,2] Bimekizumab selectively binds to and neutralizes both IL-17A and IL-17F.

Methods: BE READY (NCT03410992) was a randomized, double-blinded, placebo-controlled, pivotal phase 3 study with randomized withdrawal. 435 patients with moderate to severe psoriasis were randomized 4:1 to bimekizumab 320 mg every 4 weeks (Q4W) or placebo. Week 16 PASI 90 responders (patients who achieved a 90% improvement from baseline in Psoriasis Area and Severity Index) were re-randomized 1:1:1 to bimekizumab 320 mg every 8 weeks (Q8W) (n=100), Q4W (n=106), or placebo (n=105) through Week 56. Relapse was defined as failure to achieve PASI 75 at any visit from Week 20. Co-primary endpoints were PASI 90 and an Investigator's Global Assessment (IGA) score of 0 or 1 at Week 16. Secondary/other outcomes included PASI 100 at Week 16; PASI 90, IGA 0/1, and PASI 100 at Week 56; and safety. Missing data were imputed using non-responder imputation.

Results: At Week 16, significantly more patients achieved PASI 90 (90.8% vs 1.2%), IGA 0/1 (92.6% vs 1.2%), and PASI 100 (68.2% vs 1.2%) with bimekizumab than placebo, respectively ($p<0.001$). At Week 56, PASI 90 (320 mg Q4W/Q8W 91.0%, Q4W/Q4W 86.8%) and IGA 0/1 (320 mg Q4W/Q8W 90.0%, Q4W/Q4W 86.8%) responses were maintained on bimekizumab. At Week 56, 83.0% (320 mg Q4W/Q8W) and 70.8% (320 mg Q4W/Q4W) of patients treated with bimekizumab achieved PASI 100. At Week 56 PASI 90 was reduced (16.2%) in patients re-randomized to placebo; median time to relapse was approximately 28 weeks. The most common treatment-emergent adverse events in patients treated with bimekizumab were nasopharyngitis, oral candidiasis, and upper respiratory tract infection.

Conclusion: In this pivotal phase 3 withdrawal study, bimekizumab provided significantly higher response rates compared with placebo at Week 16. Responses were maintained through Week 56 with continuous bimekizumab treatment. Bimekizumab was generally well tolerated, with no unexpected safety findings.

References: 1. Johnston A. *J Immunol* 2013;190:2252–62. 2. Fujishima S. *Arch Dermatol Res* 2010;302:499–505.

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Novartis, Menlo, Sanofi, Sienna, Sun Pharma, Pfizer, UCB Pharma, Valeant; **AP:** Worked as an investigator and/or speaker and/or advisor for AbbVie, Almirall Hermal, Amgen, Biogen, Boehringer Ingelheim, Celgene, GSK, Eli Lilly, Galderma, Hexal, Janssen, LEO Pharma, MC2, Medac, Merck Serono, Mitsubishi, Merck Sharp and Dohme, Novartis, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Schering-Plough, UCB Pharma; KR: 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 Inc., Eli Lilly, Forward Pharma, Fresenius Medical Care, Galapagos, GSK, Janssen-Cilag, Kyowa Kirin, LEO Pharma, Medac, Merck Sharp and Dohme, Miltenyi Biotec, Novartis, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Sun Pharma, Takeda, UCB Pharma, Valeant, Xenoport; **RV:** Consultant, and/or scientific advisor, and/or investigator, and/or speaker for Amgen, AbbVie, Astellas, Bausch Health/Valeant, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Dermira Inc., Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Merck Sharp and Dohme, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharma, Takeda, UCB Pharma; **VV, CM, LP:** Employees of UCB Pharma; **AB:** Served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Allergan, Almirall, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira Inc., Eli Lilly, Forte, Galderma, Janssen, LEO Pharma, Novartis, Ortho, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, UCB Pharma; paid speaker for AbbVie.

Efficacy and Safety of Bimekizumab in Patients with Moderate to Severe Plaque Psoriasis: Results from BE VIVID, a 52-Week Phase 3, Randomized, Double-Blinded, Ustekinumab- and Placebo-Controlled Study

Kristian Reich,[1] Kim A. Papp,[2] Andrew Blauvelt,[3] Richard Langley,[4] April Armstrong,[5] Richard B. Warren,[6] Kenneth Gordon,[7] Joseph F. Merola,[8] Cynthia Madden,[9] Maggie Wang,[9] Veerle Vanvoorden,[10] Mark Lebwohl[11]

[1]Center for Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf and Skinflammation® Center, Hamburg, Germany; [2]Probity Medical Research and K Papp Clinical Research, Waterloo, Ontario, Canada; [3]Oregon Medical Research Center, Portland, OR, USA; [4]Dalhousie University, Halifax, Nova Scotia, Canada; [5]Keck School of Medicine of USC, Dermatology, Los Angeles, CA, USA; [6]The Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, University of Manchester, Manchester, UK; [7]Medical College of Wisconsin, Milwaukee, WI, USA; [8]Department of Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; [9]UCB Pharma, Raleigh, NC, USA; [10]UCB Pharma, Brussels, Belgium; [11]Icahn School of Medicine, New York, NY, USA

Introduction: Increasing evidence indicates that interleukin (IL)-17A and IL-17F contribute to the immunopathogenesis of psoriasis, a mainly Th17-driven disease.1,2 Bimekizumab selectively binds and neutralizes IL-17A and IL-17F.

Methods: In BE VIVID (NCT03370133), 567 patients with moderate to severe psoriasis were randomized 4:2:1 to bimekizumab (320 mg every 4 weeks [Q4W]), ustekinumab (45/90 mg weight-based at baseline and Week 4, then every 12 weeks [Q12W]), or placebo (Q4W through Week 16, then bimekizumab 320 mg Q4W). Co-primary endpoints were a 90% improvement from baseline in Psoriasis Area and Severity Index (PASI 90) and an Investigator's Global Assessment (IGA) score of 0 or 1 vs placebo at Week 16. Secondary/other outcomes included PASI 100 at Week 16; PASI 90, IGA 0/1 and PASI 100 at Week 52; and safety. Missing data were imputed using non-responder imputation.

Results: Significantly more patients achieved PASI 90 and IGA 0/1 at Week 16 with bimekizumab (85.0% and 84.1%, respectively) than ustekinumab (49.7% and 53.4%) or placebo (4.8% and 4.8%); all $p<0.001$. 58.6% of patients treated with bimekizumab achieved PASI 100, compared with 20.9% with ustekinumab and 0% with placebo. At Week 52, bimekizumab-treated patients achieved PASI 90, IGA 0/1, and PASI 100 response rates of 81.6%, 77.9%, and 64.2%, respectively, compared with 55.8%, 60.7%, and 38.0% with ustekinumab. Over 52 weeks, incidence of serious treatment-emergent adverse events (TEAEs) was 6.1% with bimekizumab, compared with 7.4% with ustekinumab. Four deaths occurred (two patients treated with bimekizumab, one with ustekinumab, and one with placebo), which were considered unrelated to treatment. The most common TEAEs in patients treated with bimekizumab were nasopharyngitis and oral candidiasis.

Conclusion: Bimekizumab was consistently superior to ustekinumab and placebo, and was generally well tolerated with a safety profile consistent with earlier phase 2 studies, further supporting dual neutralization of IL-17A and IL-17F for treatment of psoriasis.

References: 1. Durham L. *Curr Rheumatol Reports* 2015;17:55. 2. Fujishima S. *Arch Dermatol Res* 2010;302:499–505.

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Roflumilast Cream (ARQ-151) Improved Itch Severity and Itch-related Sleep Loss in Adults With Chronic Plaque Psoriasis in a Phase 2b Study

[1]L Stein Gold, [2]MG Lebwohl, [3]KA Papp, [4]MJ Gooderham, [2]LH Kircik, [5]ZD Draelos, [6]SE Kempers, [7]DM Pariser, [8]J Alonso-Llamazares, [9]DP Toth,[10]K Smith,

10RC Higham,10L Navale, 10H Welgus, 10DR Berk

[1]Henry Ford Medical Center, MI; [2]Icahn School of Medicine at Mount Sinai, NY; [3]Probity Medical Research and K Papp Clinical Research, ON, Canada; [4]SkiN Centre for Dermatology, ON, Canada; [5]Dermatology Consulting Services, NC; [6]Minnesota Clinical Study Center, MN; [7]Eastern Virginia Medical School and Virginia Clinical Research, Inc., VA; [8]Driven Research LLC, FL; [9]XLR8 Medical Research, Probity Medical Research, ON, Canada; [10]Arcutis Biotherapeutics, Inc., CA

Introduction: Roflumilast cream (ARQ-151), a potent phosphodiesterase-4 (PDE-4) inhibitor, is being investigated for once-daily topical treatment of chronic plaque psoriasis (PsO). A bothersome symptom of PsO is itch, which may be severe and may negatively impact quality of life. A Phase 2b trial evaluated the efficacy and safety of 2 doses of roflumilast in patients with PsO. The effect of roflumilast cream on various patient reported outcomes related to itch was also assessed.

Methods: A Phase 2b, double-blinded trial randomized adults with PsO 1:1:1 to once-daily treatment with roflumilast 0.3%, roflumilast 0.15%, or vehicle for 12 weeks. At baseline, patients had to score ≥2 on the Investigator Global Assessment (IGA) scale and ≥2 on the modified Psoriasis Area and Severity Index. The primary endpoint was achievement of clear or almost clear skin based on IGA 0 or 1 at Week 6. Throughout the trial, itch was evaluated via the Worst Itch Numeric Rating Scale (WI–NRS), Psoriasis Symptom Diary (PSD; Items 1 and 2), and Itch-related Sleep Loss score.

Results: Overall, 331 patients were randomized (109 to roflumilast 0.3%, 113 to roflumilast 0.15%, and 109 to vehicle). At baseline, the mean WI–NRS score was 5.87 and mean Itch related Sleep Loss score was 3.10. Both roflumilast doses showed similar improvements in WI–NRS score and were significantly superior to vehicle throughout the trial ($P \leq 0.002$). Among patients with a WI–NRS score ≥6 at baseline (n=197/331), rates of achievement of a ≥4 point reduction from baseline in WI–NRS score were significantly greater with roflumilast 0.3% vs vehicle at all timepoints ($P \leq 0.034$), and significantly greater with roflumilast 0.15% vs vehicle at Weeks 6 and 12 ($P \leq 0.012$). Robust improvements in severity and impact of itch based on Items 1 and 2 of the PSD were observed for both roflumilast doses at Weeks 2 through 12 ($P \leq 0.012$ vs vehicle). Improvements in the Itch-related Sleep Loss score were significantly greater with both roflumilast doses vs vehicle at Weeks 6 through 12 ($P \leq 0.022$).

Discussion: Treatment with roflumilast cream resulted in rapid and robust improvement in the severity and impact of itch associated with PsO. These data suggest that once-daily roflumilast cream, a potent PDE-4 inhibitor, may be an effective, safe, and well tolerated non steroidal topical treatment for PsO with early onset of action.

Roflumilast Cream (ARQ-151) 0.15% and 0.3% Improved Symptom Burden in Adults with Chronic Plaque Psoriasis in a Phase 2b Study

[1]LH Kircik, [1]MG Lebwohl, [2]KA Papp, [3]MJ Gooderham, [4]L Stein Gold, [5]ZD Draelos, [6]SE Kempers, [7]SK Tyring, [8]LE Albrecht, [9]M Wiseman, [10]LK Ferris, [11]K Smith, [11]RC Higham, [11]L Navale, [11]H Welgus, [11]DR Berk

[1]Icahn School of Medicine at Mount Sinai, NY; [2]Probity Medical Research and K Papp Clinical Research, ON, Canada; [3]SkiN Centre for Dermatology, ON, Canada; [4]Henry Ford Medical Center, MI; [5]Dermatology Consulting Services, NC; [6]Minnesota Clinical Study Center, MN; [7]McGovern Medical School, University of Texas Health Science Center, TX; [8]Probity Medical Research and Enverus Medical Research, BC, Canada; [9]Probity Medical Research and Skinwise

Dermatology, MB, Canada; [10]Univeristy of Pittsburgh, PA; [11]Arcutis Biotherapeutics, Inc., CA

Introduction: Plaques resulting in pain, itching, or burning are typical signs of chronic plaque psoriasis (PsO) and can have negative effect on quality of life. Roflumilast cream (ARQ-151) is a potent phosphodiesterase-4 (PDE-4) inhibitor in clinical development for once-daily topical treatment of PsO. A Phase 2b trial evaluated the efficacy and safety of 2 doses of roflumilast. The effect of roflumilast cream on patient reported outcomes, including psoriasis symptom burden and quality of life, was also assessed.

Methods: A Phase 2b, double-blinded trial randomized adults with PsO 1:1:1 to once-daily treatment with roflumilast 0.3%, roflumilast 0.15%, or vehicle for 12 weeks. At baseline, patients had to score ≥2 on the Investigator Global Assessment (IGA) scale and ≥2 on the modified Psoriasis Area and Severity Index. The primary endpoint was achievement of clear or almost clear skin based on IGA 0 or 1 at Week 6. Patients completed the Psoriasis Symptom Diary (PSD) assessing the severity and impact of stinging, burning, skin cracking, pain, and scaling. The Dermatology Life Quality Index (DLQI) was completed by a subset of patients (n=180).

Results: In total, 331 patients were randomized: 109 to roflumilast 0.3%, 113 to roflumilast 0.15%, and 109 to vehicle. Rapid and statistically significant improvements on the total PSD score were observed at Weeks 4–12 for the 0.3% dose ($P \leq 0.002$ vs vehicle) and as early as Week 2 for the 0.15% dose ($P \leq 0.014$). Statistically significant improvements for both roflumilast doses versus vehicle were seen in burden of individual patient-reported symptoms of scaling by Week 2; stinging, skin cracking, and pain by Week 4; and burning by Week 6. All reported improvements in individual symptoms were maintained through Week 12. Mean change in DLQI score from baseline at Week 12 was significantly greater for both roflumilast doses versus vehicle ($P \leq 0.036$). Improvements in DLQI occurred as early as Week 6 for roflumilast 0.3% ($P=0.045$ vs vehicle) and Week 8 for roflumilast 0.15% ($P=0.013$).

Discussion: Both doses of once-daily roflumilast cream led to rapid and robust improvements in symptom burden and quality of life in adults with PsO. Once-daily roflumilast cream, a potent, PDE-4 inhibitor, may be an effective, safe, and well-tolerated non-steroidal topical treatment for PsO with early onset of action.

The Safety and Efficacy of Roflumilast Cream 0.15% and 0.05% in Atopic Dermatitis: Phase 2 Proof-of-Concept Study

[1]MJ Gooderham, [2]LH Kircik, [3]M Zirwas, [4]M Lee, [5]SE Kempers, [6]ZD Draelos, [7]LK Ferris, [8]TM Jones, [9]E Saint-Cyr Proulx, [9]R Bissonnette, [10]N Bhatia, [11]ST Guenthner, [12]RA Koppel, [13]H Welgus, [13]C Merritt, [13]M Elias, [13]L Navale, [13]RC Higham, [13]M Droege, [13]DR Berk

[1]SKiN Centre for Dermatology, ON, Canada; [2]Icahn School of Medicine at Mount Sinai, NY; [3]Dermatologists of the Central States, OH; [4]Progressive Clinical Research, TX; [5]Minnesota Clinical Study Center, MN; [6]Dermatology Consulting Services, PLLC, NC; [7]University of Pittsburgh, PA; [8]US Dermatology Partners, TX; [9]Innovaderm Research, QC, Canada; [10]Therapeutics Clinical Research, CA; [11]The Dermatology Center of Indiana, IN; [12]Tulane University School of Medicine in New Orleans, LA; [13]Arcutis Biotherapeutics, Inc., CA

Introduction: Roflumilast cream (ARQ 151) is a highly potent phosphodiesterase-4 (PDE-4) inhibitor with ~25- to >300-fold higher potency than the approved PDE-4 inhibitors, crisaborole and apremilast. Roflumilast is in development for plaque psoriasis and atopic dermatitis (AD). The objective of this Phase 2, proof of concept study was to assess the safety and efficacy of once daily roflumilast cream 0.15% and 0.05% in patients with mild to moderate AD.

Methods: This randomized, parallel-group, double-blind, vehicle controlled study enrolled 136 patients (≥12 years of age) from North America who had 1.5–35% body surface area (BSA) affected by AD, with a validated investigator global assessment AD (vIGA-AD) score of 2 (mild) or 3 (moderate), and eczema area and severity index (EASI) score of ≥5. Patients were randomized to roflumilast 0.15%, roflumilast 0.05% or vehicle once-daily for 4 weeks. The primary efficacy endpoint was absolute change from baseline in EASI score at Week 4.

Results: At baseline, 22.1% of patients had a vIGA-AD of mild, 77.9% had a vIGA AD of moderate, and mean BSA was 9.5%. At Week 4, the mean changes in EASI scores were 6.4 ($P=0.097$ compared with vehicle), 6.0 ($P=0.356$), and 4.8 with roflumilast 0.15%, roflumilast 0.05%, and vehicle, respectively (primary endpoint). Statistically significant improvements compared with vehicle were observed at Week 4 for % change from baseline in EASI score (72.3% [$P=0.049$], 69.4% [$P=0.164$], and -55.8% for roflumilast 0.15%, roflumilast 0.05%, and vehicle, respectively); patients reaching EASI 75 (52.3% [$P=0.045$], 59.1% [$P=0.009$], and 31.1%); and patients achieving vIGA-AD score of clear or almost clear (52.3% [$P=0.040$], 50.0 [$P=0.076$], and 31.1%). Overall, 4 patients experienced a treatment-related adverse event (AE): none in roflumilast 0.15%, 2 in roflumilast 0.05%, and 2 in vehicle group. Only 2 patients discontinued study drug due to an AE. Application site pain was reported in 2 patients: 1 in roflumilast 0.05% and 1 in vehicle group.

Discussion: In this small study, the primary endpoint showed a trend towards, but did not reach, statistical significance. However, statistical significance was reached for other efficacy endpoints. Both doses of roflumilast had a favorable safety profile, with a low rate of application site reactions. This study suggests that roflumilast cream, a potent PDE-4 inhibitor, represents a potential effective once-daily treatment for AD.

Deucravacitinib (BMS-986165), an Oral, Selective Tyrosine Kinase 2 Inhibitor: Evaluation of Changes in Laboratory Parameters in Response to Treatment in a Phase 2 Trial in Psoriasis Patients

Kenneth Gordon,[1] Kim Papp,[2] Melinda Gooderham,[3] Akimichi Morita,[4] Peter Foley,[5] Diamant Thaçi,[6] Sudeep Kundu,[7] Renata Kisa,[7] Lan Wei,[7] Subhashis Banerjee[7]

[1]Medical College of Wisconsin, Milwaukee, WI, USA; [2]Clinical

Research and Probity Medical Research Inc, Waterloo, ON, Canada; [3]SKiN Centre for Dermatology, Queen's University and Probity Medical Research, Peterborough, ON, Canada; [4]Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; [5]The University of Melbourne, St Vincent's Hospital Melbourne & Probity Medical Research, Skin & Cancer Foundation Inc, Melbourne, VIC, Australia; [6]University of Lübeck, Lübeck, Germany; 7Bristol Myers Squibb, Princeton, NJ, USA

Background: In a Phase 2 trial of the oral, selective tyrosine kinase 2 (TYK2) inhibitor deucravacitinib (BMS-986165) in patients with moderate to severe plaque psoriasis (NCT02931838),[1] 67% to 75% achieved PASI 75 (≥75% reduction from baseline on the Psoriasis Area and Severity Index) at Week 12 at doses of ≥3 mg twice daily (BID) versus 7% with placebo (P<0.001), with an acceptable adverse event profile. We investigated the effect of deucravacitinib on standard laboratory parameters, many of which become abnormal on treatment with other kinase inhibitors.

Methods: Patients were randomized to 1 of 5 doses of deucravacitinib or placebo for 12 weeks. Mean absolute values (with associated SD) in hematologic, hepatic, and lipid (total cholesterol, triglycerides) parameters; creatinine, creatine phosphokinase (CPK) and glucose levels; blood pressure; and weight/body mass index were assessed for the 3 most effective doses (3 mg BID, 6 mg BID, and 12 mg once daily [QD]) and placebo.

Results: In total, 267 patients were randomized. Most laboratory parameters stayed within normal range during treatment, including hematologic (lymphocytes, neutrophils, platelets, hemoglobin), liver enzymes, creatinine, glucose, and lipid panel. CPK levels were elevated in placebo (baseline: 142.6 U/L [SD, 91.3]; Week 12: 155.5 U/L [88.8]) and treatment groups (baseline: 3 mg BID: 130.0 U/L [99.6], 6 mg BID: 143.6 U/L [159.8], 12 mg QD: 143.6 U/L [86.6]; Week 12: 3 mg BID: 139.7 U/L [106.2], 6 mg BID: 156.1 U/L [137.9], 12 mg QD: 194.5 U/L [357.8]). The CPK increases were asymptomatic, mostly adverse event grades 1 or 2, and were observed in 12/44 patients (27%) who received placebo and 57/221 (26%) who received deucravacitinib. Safety results were not dose-dependent and no events resulted in discontinuation from the study.

Conclusion: No consistent differences between placebo and treated groups and no clear dose-dependence were seen in laboratory parameters investigated. Results of ongoing Phase 3 trials of deucravacitinib in psoriasis (NCT03624127, NCT03611751, NCT04167462, NCT03924427) will provide long-term safety and laboratory data.

Reference: 1. Papp K et al. *N Engl J Med.* 2018;379:1313-1321.

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DT: Research support/principal investigator (clinical trials): AbbVie, Almirall, Amgen, Biogen Idec, Boehringer

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Deucravacitinib (BMS-986165), an Oral Selective TYK2 Inhibitor, in the Treatment of Moderate to Severe Psoriasis as Assessed by the Static Physician's Global Assessment (sPGA)/Body Surface Area (BSA) Composite Tool (sPGAxBSA), a Clinically Useful Alternative to PASI

Alice B. Gottlieb,[1] Bruce Strober,[2] Diamant Thaçi,[3] Kenneth Gordon,[4] Sudeep Kundu,[5] Renata Kisa,[5] Lan Wei,[5] Subhashis Banerjee,[5] Joseph F. Merola[6]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Yale University, New Haven, CT, and Central Connecticut Dermatology Research, Cromwell, CT, USA; [3]University of Lübeck, Lübeck, Germany; [4]Medical College of Wisconsin, Milwaukee, WI, USA; [5]Bristol Myers Squibb, Princeton, NJ, USA; [6]Harvard Medical School, Boston, MA, USA

Introduction: In a Phase 2 trial of the oral, selective tyrosine kinase 2 (TYK2) inhibitor deucravacitinib (BMS-986165), in 267 patients with moderate to severe plaque psoriasis (NCT02931838), 67%–75% achieved PASI 75 at Wk12 (primary endpoint) at doses ≥3 mg twice daily (BID) versus 7% with placebo (P<0.001).1 The product of sPGA and BSA (sPGA×BSA) accounts for the extent and severity of psoriasis and may be a simple, clinically useful alternative to PASI.2–5

Methods: This post hoc analysis of the Phase 2 trial evaluated sPGA×BSA for assessing response to deucravacitinib. Patients were randomized (n=44–45/group) to 1 of 5 oral BMS-986165 doses (3 mg every other day, 3 mg once daily [QD], 3 mg BID, 6 mg BID, 12 mg QD) or placebo. Assessments included: PASI, sPGA, BSA, and Dermatology Life Quality Index (DLQI).1 Spearman correlation coefficients (corr) for all treatment groups evaluated sPGA×BSA and PASI relationship at baseline and Wk12. Agreement was based on concordance rates.

Results: All randomized patients were assessed. Percentage change from baseline to Wk12 was similar for sPGA×BSA and PASI in deucravacitinib treatment groups and the placebo group. At Wk12, sPGA×BSA correlated strongly with PASI (corr=0.94) and moderately with DLQI (corr=0.58) across all treatment groups. A 75% reduction in sPGA×BSA and PASI was achieved by similar proportions of patients receiving the most effective deucravacitinib doses (≥3 mg BID) (sPGA×BSA 75: 78.4%; PASI 75: 70.1%) and by similar proportions of placebo recipients (sPGA×BSA 75: 13.3%; PASI 75: 6.7%).

Conclusion: In patients with moderate to severe psoriasis, PASI strongly correlated with sPGA×BSA at Wk12 in all deucravacitinib treatment groups and placebo, further supporting sPGA×BSA as a simple, accurate, convenient alternative to PASI.

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SK, RK, LW, SB: employees and shareholders: Bristol Myers Squibb Company.

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An Oral, Selective Tyrosine Kinase 2 Inhibitor, Deucravacitinib (BMS-986165), Reduced Absolute Psoriasis Area and Severity Index in a Phase 2 Trial in Psoriasis

Bruce Strober,[1] Alice B. Gottlieb,[2] Diamant Thaçi,[3] Luis Puig,[4] Matthew J. Colombo,[5] Sudeep Kundu,[5] Renata Kisa,[5] Subhashis Banerjee[5]

[1]Yale University, New Haven, CT, and Central Connecticut Dermatology Research, Cromwell, CT, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Research Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany; [4]Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain; [5]Bristol Myers Squibb, Princeton, NJ, USA

Background: Although a consensus therapeutic target has yet to be defined, a recent analysis reported that attainment of an absolute Psoriasis Area and Severity Index (PASI) ≤2 translates to meaningful improvements in clinical and health-related quality of life outcomes in patients with plaque psoriasis.[1] Deucravacitinib (BMS-986165) is an oral, selective inhibitor of tyrosine kinase 2, an intracellular enzyme involved in key cytokine signaling pathways implicated in the pathogenesis of psoriasis. In a Phase 2, double-blind trial in moderate to severe plaque psoriasis, 67% to 75% of patients treated with deucravacitinib at doses of 3 or 6 mg twice daily (BID) or 12 mg once daily (QD) achieved PASI 75 at Week 12 (primary endpoint) versus 7% with placebo (P<0.001; NCT02931838).[2] The current post hoc analysis of this trial compared the efficacy of deucravacitinib versus placebo based on absolute PASI over time and at Week 12.

Methods: Adults with moderate to severe plaque psoriasis were randomized equally to 1 of 5 deucravacitinib doses or placebo. Mean change from baseline in absolute PASI through Week 12 and percentage of patients at Week 12 who achieved an absolute PASI of ≤1, ≤2, ≤3, and ≤5 were determined for the 3 highest dose groups (3 mg BID, 6 mg BID, 12 mg QD; n=134) versus placebo (n=45).

Results: Baseline demographics and disease characteristics, including baseline PASI, were similar across dose groups. Deucravacitinib was associated with greater reductions from baseline in absolute PASI than placebo, with separation from placebo apparent as early as Week 1. The percentages of patients with absolute PASI ≤1 (30.6 vs 0), ≤2 (47.0 vs 0), ≤3 (58.2 vs 2.2), and ≤5 (71.6 vs 8.9) at Week 12 were higher in the combined deucravacitinib group compared with the placebo group. Similar results were obtained for each of the individual deucravacitinib dose groups. Approximately 50% of deucravacitinib treated patients achieved an absolute PASI ≤2.

Conclusions: Deucravacitinib elicits a rapid response and is efficacious in achieving absolute PASI treatment outcomes that are clinically meaningful in patients with moderate to severe plaque psoriasis. Five Phase 3 trials in plaque psoriasis (NCT03624127, NCT03611751, NCT04167462, NCT03924427, and NCT04036435) are currently evaluating the efficacy and safety of deucravacitinib over a longer treatment period in larger patient cohorts.

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Efficacy and Safety of Ruxolitinib Cream for the Treatment of Atopic Dermatitis: Results From Two Phase 3, Randomized, Double-Blind Studies

Kim Papp, MD, PhD,[1] Jacek C. Szepietowski, MD, PhD,[2]

Leon Kircik, MD,[3] Darryl Toth, MD,[4] Michael E. Kuligowski, MD, PhD, MBA,[5] May E. Venturanza, MD,5 Kang Sun, PhD,[5] Eric L. Simpson, MD[6]

[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]Incyte Corporation; [6]Oregon Health and Science University

Introduction: Atopic dermatitis (AD) is a chronic, intensely pruritic inflammatory skin disease. Janus kinases (JAKs) act downstream of key proinflammatory cytokines and itch mediators involved in AD pathogenesis. Ruxolitinib selectively inhibits JAK1 and JAK2. Here we report efficacy and safety data of ruxolitinib cream from the initial 8 weeks of two phase 3 AD studies.

Methods: Two identical studies (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]) enrolled patients aged ≥12 years with AD, an Investigator's Global Assessment (IGA) score of 2 or 3, and 3%–20% affected body surface area. In both studies, patients were randomized 2:2:1 to 0.75% ruxolitinib cream, 1.5% ruxolitinib cream, and vehicle (all twice daily) for 8 continuous weeks. Patients on ruxolitinib subsequently continued treatment for 44 weeks; patients initially randomized to vehicle were rerandomized 1:1 to either ruxolitinib regimen. The primary endpoint was IGA treatment success (IGA-TS) at Week 8 (IGA of 0 or 1 and a ≥2-grade improvement from baseline). Secondary endpoints at Week 8 vs baseline included ≥75% improvement in Eczema Area and Severity Index (EASI-75), a ≥4-point improvement in itch Numerical Rating Scale score (NRS4), and safety.

Results: In TRuE-AD1/TRuE-AD2, 631/618 patients were randomized (vehicle, n=126/124; 0.75% ruxolitinib, n=252/248; 1.5% ruxolitinib, n=253/246); the median (interquartile range) age was 32.0 (19–49)/33.0 (20–52) years, 62.0%/61.5% were female, and 19.5%/19.7% were adolescents. In TRuE-AD1 and TRuE-AD2, significantly more patients treated with either ruxolitinib strength achieved IGA-TS (0.75% ruxolitinib, 50.0%/39.0%; 1.5% ruxolitinib, 53.8%/51.3%) vs vehicle (15.1%/7.6%; all P<0.0001). EASI-75 was achieved by 56.0%/51.5% of patients applying 0.75% ruxolitinib and 62.1%/61.8% on 1.5% ruxolitinib vs 24.6%/14.4% on vehicle (all P<0.0001) in TRuE-AD1 and TRuE-AD2. In both studies, significantly greater itch reduction occurred within 12 hours of the first application of 1.5% ruxolitinib vs vehicle (P<0.05). At Week 8, NRS4 was achieved by more patients who applied ruxolitinib (0.75% ruxolitinib, 40.4%/42.7%; 1.5% ruxolitinib, 52.2%/50.7%) vs vehicle (15.4%/16.3%, all P<0.001). During the 8-week vehicle-controlled period, 15 patients discontinued from the studies because of a treatment-emergent adverse event (TEAE; vehicle, n=8 [3.2%]; 0.75% ruxolitinib, n=4 [0.8%]; 1.5% ruxolitinib, n=3 [0.6%]). No serious TEAEs were considered related to ruxolitinib treatment, and there were no TEAEs suggestive of a relationship to its bioavailability.

Conclusions: Ruxolitinib cream demonstrated anti-inflammatory and antipruritic effects with superior efficacy vs vehicle for IGA-TS, EASI-75, and itch NRS4. The safety profile was similar to vehicle and consistent between both studies. These results support the potential of ruxolitinib cream as an effective and well-tolerated topical treatment for AD (Funding, Incyte Corporation).

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Early and Maintained Response Levels in Psoriasis Patients Treated with Tildrakizumab

Kim Papp,[1] Jensen Yeung,[2] Neil Shear,[3] Lorne Albrecht,[4] Charles Lynde,[5] Jingchuan Zhang,[6] Yang Zhao,[6] Alan M Mendelsohn,[6] Melinda Gooderham[7]

[1]K. Papp Clinical Research, and Probity Medical Research, Waterloo, ON, CA; [2]Women's College Hospital and Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, CA; and Probity Medical Research, Waterloo, ON, CA; [3]Division of Dermatology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, CA; [4]Enverus Medical and Probity Medical Research, Surrey, BC, Canada; [5]Department of Medicine, University of Toronto, Toronto, ON, CA; [6]Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA; [7]Probity Medical Research, and SKiN Centre for Dermatology, Peterborough, ON, Canada; and Queen's University, Kingston, ON, CA

Introduction: Tildrakizumab is approved in the US, Europe, Australia, and Japan to treat adult patients with plaque psoriasis. We investigated long-term efficacy of tildrakizumab from baseline to week (W)148 among patients achieving various Psoriasis Area and Severity Index (PASI) responses at W28.

Methods: This was a post hoc analysis of pooled data from reSURFACE 1 and reSURFACE 2 (NCT01722331/NCT01729754). Part 1 (0–12 weeks) of these trials was placebo controlled. Part 2 (12–28 weeks) re-randomized placebo patients to tildrakizumab 100 or 200 mg. In Part 3 (28–64/52 weeks in reSURFACE 1/2), patients with PASI ≥50 were re-randomized to placebo, or to continue or increase their dose; patients with PASI <50 were discontinued. Patients who received tildrakizumab within 12 weeks and achieved PASI ≥50 at the end of Part 3 were eligible to enroll in the long-term extension (LTE). This analysis included patients treated with tildrakizumab 100 mg in Parts 1–3 (at W0, W4, and every 12 weeks after) and at least one dose during the LTE. Patients were classified into 4 mutually exclusive groups based on their W28 PASI response: PASI 50–74, 75–89, 90–99, and 100. Percent PASI improvement from baseline to W148 was examined for each PASI group using both observed data and imputed data with last observation carried forward.

Results: This analysis included 335 tildrakizumab patients: 34, 79, 131, and 91 patients in the W28 PASI 50–74, 75–89, 90–99, and 100 groups, respectively. Response curves for these PASI groups were unique. Mean PASI improvements at W4 were 27.1%, 36.6%, 44.7%, and 52.5% for W28 PASI 50–74, 75–89, 90–99, and 100 groups, respectively. Among patients achieving PASI 75–89, 90–99, and 100 at W28, mean PASI improvements were sustained up to 148 weeks: 85.3%, 92.4%, and 95.4% for the 3 groups, respectively. Patients achieving W28 PASI 50–74 had continuous mean PASI improvement from W28 (64.4%) to W52 (79.4%) and W64 (82.2%), which were

further sustained through 148 weeks (81.4%).

Conclusions: Patients who received tildrakizumab and achieved PASI ≥90 at W28 had rapid improvements as early as W4. Among patients achieving W28 PASI ≥50, PASI improvements were improved or sustained through 148 weeks.

Disclosures: Merck Sharp & Dohme Corp. funded the studies; Sun Pharmaceutical Industries, Inc. the analyses.

Tildrakizumab Efficacy by Metabolic Syndrome Status in Psoriasis: Post Hoc Analysis of 3-Year Data from the Phase 3 reSURFACE 1 and reSURFACE 2 Studies

Mark G Lebwohl,[1] Nehal N Mehta,[2] Alice B Gottlieb,[3] Alan M Mendelsohn,[4] Stephen J Rozzo,[4] M Alan Menter[5]

[1]Department of Dermatology, Mount Sinai Hospital, New York, NY, USA; [2]National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD, USA; [3]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA; [5]Division of Dermatology, Baylor Scott & White, and Texas A&M College of Medicine, Dallas, TX, USA

Introduction: Metabolic syndrome (MetS) may reduce absolute Psoriasis Area and Severity Index (PASI) response and long-term drug survival in patients with psoriasis. Tildrakizumab (TIL) is approved for treatment of moderate to severe plaque psoriasis. This is an updated 3-year post hoc analysis of TIL efficacy from the phase 3 reSURFACE 1 and reSURFACE 2 (NCT01722331/NCT01729754) studies in patients with psoriasis with vs without MetS by National Cholesterol Education Program-Adult Treatment Panel III criteria.

Methods: Patients ≥18 years with moderate to severe chronic plaque psoriasis received TIL 100 or 200 mg at week (W)0, W4, and every 12 weeks thereafter up to W220/W244 (reSURFACE 1/2); additional patients in reSURFACE 2 received etanercept twice weekly to W16 and once weekly to W28. Proportion of patients with ≥75% improvement from baseline in PASI (PASI 75) and change in PASI from baseline to W148 were assessed.

Results: Of patients continuously receiving TIL 100/200 mg, 21%/23% had MetS in reSURFACE 1; 21%/19% had MetS in reSURFACE 2. Patients with vs without MetS had higher median baseline weight, body mass index, and prevalence of cardiovascular disease and diabetes mellitus. Proportions of patients receiving TIL 100 mg with vs without MetS achieving PASI 75 in reSURFACE 1/2 were comparable at W52 (85%/86% vs 86%/94%), W100 (65%/77% vs 76%/88%), and W148 (69%/73% vs 71%/79%). Among patients receiving TIL 200 mg, proportions of PASI 75 responders with vs without MetS were also similar at W52 (76%/87% vs 76%/87%), W100 (68%/73% vs 81%/85%), and W148 (71%/63% vs 74%/81%). At W148, overall PASI scores decreased from baseline by 89%/93% vs 92%/96% (TIL 100 mg) and 88%/84% vs 91%/94% (TIL 200 mg) in patients with vs without MetS (reSURFACE 1/2, respectively).

Conclusions: Efficacy of both TIL doses was maintained over 148 weeks and was comparable in patients with vs without MetS.

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Efficacy and Safety of Tildrakizumab, a High-Affinity Anti–Interleukin-23P19 Monoclonal Antibody, in Patients with Active Psoriatic Arthritis

Philip J Mease,[1] Saima Chohan,[2] Ferran J García Fructuoso,[3] Alice B Gottlieb,[4] Proton Rahman,[5] Siba P Raychaudhuri,[6] Richard C Chou,[7] Alan M Mendelsohn,[8] Stephen J Rozzo,[8] Cynthia Trickett,[9] Melodie Young,[10] Michael E Luggen[11]

[1]Swedish Medical Centre/Providence St. Joseph Health and University of Washington, Seattle, WA, USA; [2]Arizona Arthritis and Rheumatology Research, PLLC, Phoenix, AZ; [3]Hospital CIMA Sanitas, Barcelona, Spain; [4]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY; [5]Craig L Dobbin Genetics Research Centre, Memorial University, St. John's, NL; [6]Division of Rheumatology, Allergy & Clinical Immunology, University of California School of Medicine, Davis, and VA Medical Centre Sacramento, Sacramento, CA; [7]Division of Allergy, Immunology and Rheumatology, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, NY; [8]Sun Pharmaceutical Industries, Inc, Princeton, NJ; [9]Texas Southwestern Medical Center and University of North Texas Health Science Center, Dallas, Texas; [10]Mindful Dermatology, Modern Research Associates, Dallas, Texas; [11]Cincinnati Rheumatic Disease Study Group, Inc, and University of Cincinnati College of Medicine, Cincinnati, OH

Introduction: A randomized, double-blind, placebo-controlled, multiple-dose, phase 2b study in PsA evaluated the efficacy and safety of tildrakizumab (TIL)–a high-affinity anti–interleukin-23p19 monoclonal antibody–up to week (W)52 (NCT02980692).

Methods: Patients ≥18 years with active PsA were randomized 1:1:1:1:1 to TIL 200 mg every 4 weeks (Q4W)→W52, TIL 200 mg Q12W→W52, TIL 100 mg Q12W→W52, TIL 20 mg Q12W→W24 then TIL 200 mg Q12W→W52, or placebo (PBO) Q4W→W24 then TIL 200 mg Q12W→W52. Efficacy assessments included the proportion of patients who achieved a 20% reduction from baseline by American College of Rheumatology response criteria (ACR20) and 75% improvement in Psoriasis Area and Severity Index (PASI). Treatment-emergent adverse events (TEAEs) were monitored.

Results: Of 500 patients screened, 391 were randomized and received ≥1 dose of drug. Demographics and baseline disease characteristics were generally consistent across treatment arms. At baseline, the mean (SD) PASI score was 6.8 (8.2), 235 patients had body surface area (BSA) ≥3% at baseline, and 23.3% were anti–tumor necrosis factor-experienced. At W24, 71.4%–79.5% patients in TIL arms vs 50.6% in PBO arm achieved ACR20 ($P < 0.01$ TIL arms vs PBO). At W52, ACR20 response rates were maintained for TIL 200 mg Q4W (79.5%), 200 mg Q12W (72.2%), and 100 mg Q12W (67.5%) arms and further increased for TIL 20→00 mg Q12W (78.2%) and PBO→TIL 200 mg Q12W (77.2%) arms. Among patients with baseline BSA ≥3%,

TIL treatment significantly increased the proportion of PASI 75 responders (46.3%–79.6%) vs PBO (16.7%) at W24 (P <0.01); the proportion of responders continued to increase thereafter and was sustained through W52 including in the PBO→TIL 200 mg Q12W arm (64.3%). TEAEs and serious TEAEs occurred in 64.5% and 3.3% of patients, respectively. No deaths or major adverse cardiac events occurred.

Conclusions: TIL improved joint and skin manifestations of PsA through W52 and was well tolerated among all treatment groups.

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Efficacy and Safety of Long-Term Tildrakizumab for Plaque Psoriasis: 4-Year Results from reSURFACE 1 and reSURFACE 2

Richard G Langley,[1] Jeffrey Crowley,[2] Melinda Gooderham,[3] Kim A Papp,[4] Neil J Korman,[5] Lynda Spelman,[6] Atsuyuki Igarashi,[7] Mamitaro Ohtsuki,[8] Aditya K Gupta,[9] Paul Yamauchi,[10] Alan M Mendelsohn,[11] Stephen J Rozzo,[11] Kimberly Eads,[12] Scott Guenthner,[12] M Alan Menter[13]

[1]Division of Dermatology, Department of Medicine, Dalhousie University, Halifax, NS, Canada; [2]Bakersfield Dermatology & Skin Cancer Medical Group, Bakersfield, CA, USA; [3]Probity Medical Research and SKiN Centre for Dermatology, Peterborough, ON, Canada; Queen's University, Kingston, ON, Canada; [4]K. Papp Clinical Research, and Probity Medical Research, Waterloo, ON, Canada; [5]Case Western Reserve University and University Hospital Cleveland Center, Cleveland, OH, USA; [6]Veracity Clinical Research, Woolloongabba, Brisbane, Queensland, Australia; and Probity Medical Research, Brisbane, Australia; [7]Department of Dermatology, NTT Medical Center Tokyo, Tokyo, Japan; [8]Department of Dermatology, Jichi Medical University Hospital, Tochigi-ken, Japan; [9]Division of Dermatology, Department of Medicine, University of Toronto School of Medicine, Toronto, Canada; and Mediprobe Research Inc., London, Canada; [10]David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [11]Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA; [12]The Indiana Clinical Trials Center, Plainfield, IN, USA; [13]Division of Dermatology, Baylor Scott & White, and Texas A&M College of Medicine, Dallas, TX, USA

Introduction: Tildrakizumab (TIL) is a high-affinity, humanized, anti–interleukin-23p19 monoclonal antibody approved to treat moderate-to-severe plaque psoriasis.

Methods: reSURFACE 1/2 were double-blind, randomized, controlled studies evaluating TIL 100 and 200 mg in adults with moderate-to-severe chronic plaque psoriasis. Patients with ≥50% Psoriasis Area and Severity Index score (PASI 50) improvement at base study completion (week 64/52) could enter long-term extension at same dose. PASI response, Physician's Global Assessment (PGA) response (0 or 1 with ≥2 grade reduction), and prespecified adverse events (AEs) are presented up to week 208/200 for reSURFACE 1/2. Results: Of 638/756 patients completing the reSURFACE 1/2 base studies, 506/731 entered the extension studies (2210.8/2768.3 total patient-years [PY] follow-up). At week 208 in reSURFACE 1, 82%/56%/28% (N=178) of patients receiving TIL 100 mg and 82%/55%/27% (N=226) receiving TIL 200 mg achieved PASI 75/90/100; 58%/60% receiving TIL 100/200 mg achieved PGA response. At week 200 in reSURFACE 2, 89%/64%/35% (N=322) receiving TIL 100 mg and 89%/62%/30% (N=298) receiving TIL 200 mg achieved PASI 75/90/100; 65%/66% of patients receiving TIL 100/200 mg achieved PGA response. Long-term results were similar to at base study completion. From base study completion to week 208/200, 22%/21% receiving TIL in reSURFACE 1/2 discontinued, most due to patient withdrawal. For all prespecified AEs, exposure-adjusted rates per 100 PY for patients receiving TIL 100 or 200 mg were ≤1.1/≤1.6 in reSURFACE 1/2. Drug-related hypersensitivity, confirmed major adverse cardiac events, and malignancies occurred at ≤0.2, ≤0.7, and ≤1.3 events/100 PY, respectively, in both studies.

Conclusions: During 4 years of TIL treatment, PASI and PGA responses were high and durable, with low prespecified AE rates.

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Safety, Pharmacokinetics, and Efficacy of Efinaconazole 10% Topical Solution for the Treatment of Onychomycosis in Pediatric Patients

Lawrence F Eichenfield,[1] Boni Elewski,[2] Jeffrey L Sugarman,[3] Ted Rosen,[4] Tracey C. Vlahovic,[5] Aditya K. Gupta,[6] Linda Stein Gold,[7] Radhakrishnan Pillai,[8] Eric Guenin[9]

[1]University of California San Diego School of Medicine and Rady Children's Hospital, San Diego, CA; [2]University of Alabama at Birmingham School of Medicine, Birmingham, AL; [3]University of California, San Francisco, CA; [4]Baylor College of Medicine, Houston, TX; [5]Temple University School of Podiatric Medicine, Philadelphia, PA; [6]Mediprobe Research Inc., London, ON, CAN and University of Toronto, Toronto, ON, CAN; [7]Henry Ford Hospital, Detroit, MI; [8]Bausch Health US, LLC, Petaluma, CA; [9]Ortho Dermatologics,* Bridgewater, NJ.*

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

Introduction: Onychomycosis—a chronic fungal nail infection—is prevalent in children and responsible for approximately 15% of nail dystrophies. Treatments include topical and oral therapies, though pediatric data are limited. The objective of this study was to evaluate efinaconazole 10% topical solution in pediatric patients with onychomycosis.

Methods: This phase 4, multicenter, open-label study evaluated the safety, pharmacokinetics (PK), and efficacy of efinaconazole 10% topical solution administered once daily for 48 weeks in pediatric patients with distal lateral subungual onychomycosis. Participants were aged 6-16 years with culture-positive mild-to-severe onychomycosis affecting ≥20% of at least 1 great toenail; PK subset was patients 12-16 years with moderate-to-severe onychomycosis affecting ≥50% of both great

toenails and onychomycosis in ≥4 additional toenails.

Results: In the safety population (n=60), mean age was 13.4 years, 66.7% were male, and 88.3% were white. There were 99 treatment-emergent adverse events (TEAEs) in 38 (63.3%) participants; all TEAEs were mild or moderate and none led to study discontinuation. Most frequently reported TEAEs were nasopharyngitis (30.0%), headache (10.0%), influenza (8.3%), and tinea pedis, contusion, nail injury, and ingrowing nail (6.7% each). The only treatment-related TEAE was ingrowing nail (8 events in 2 participants). In the PK subset at week 4 (n=15), mean efinaconazole C_{max} was 0.549 ng/mL, which occurred at a median T_{max} of 12.0 hours, and mean AUC_{0-24} was 11.4 h*ng/mL. By week 52, 65.0% of patients achieved mycologic cure, defined as negative potassium hydroxide and negative fungal culture; a 36.7% mycologic cure rate was observed as early as week 12. A total of 40.0% of patients had complete cure (0% clinical involvement of target great toenail + mycologic cure) by week 52. Half of patients achieved clinical efficacy by study end, defined as affected target great toenail area <10%.

Conclusions: Efinaconazole 10% topical solution was well tolerated in this pediatric population, with similar systemic exposure and improved efficacy compared with previous adult studies.

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Long-Term Management of Moderate-to-Severe Plaque Psoriasis: Maintenance of Treatment Success Following Cessation of Halobetasol Propionate 0.01%/Tazarotene 0.045% Lotion

Linda Stein Gold, MD[1], Mark G Lebwohl, MD[2], Neal Bhatia, MD[3], Douglas DiRuggiero, PA-C[4], Abby Jacobson, MS, PA-C[5], Radhakrishnan Pillai, PhD[6]

[1]Henry Ford Hospital, Detroit, MI; [2]Icahn School of Medicine at Mount Sinai, New York, NY; [3]Therapeutics Clinical Research, San Diego, CA; [4]Skin Cancer & Cosmetic Dermatology, Rome, Georgia; [5]Ortho Dermatologics, Bridgewater, NJ; [6]Bausch Health US, LLC*, Petaluma, CA*

**Bausch Health Americas, Inc. and Bausch Health US, LLC are affiliates of Bausch Health Companies Inc. Ortho Dermatologics is a division of Bausch Health US, LLC*

Introduction: Psoriasis is an immune-mediated disease that may have frequent remissions and exacerbations. Treating psoriasis by combining tazarotene (TAZ) with a topical corticosteroid, such as halobetasol propionate (HP), may enhance efficacy while reducing side effects of HP, which limit long-term use. TAZ also sustains response posttreatment and may play a role in maintenance therapy. The objective of this analysis was to investigate maintenance of effect posttreatment following once-daily application of a fixed combination HP 0.01%/TAZ 0.045% lotion in patients with moderate-to-severe psoriasis who achieved clear skin.

Methods: This 1-year, open-label study (NCT02462083) assessed a fixed-combination, once-daily HP 0.01%/TAZ 0.045% lotion in participants with moderate-to-severe psoriasis. HP/TAZ was stopped for those achieving treatment success (Investigator's Global Assessment [IGA] score of clear [0] or almost clear [1]) at week 8; those without treatment success continued with once-daily HP/TAZ. At week 12, participants demonstrating ≥1-grade IGA improvement from baseline continued and were managed in 4-week cycles (no treatment success: continued HP/TAZ; treatment success: no treatment until next evaluation). Maximum continuous exposure was 24 weeks.

Results: Of 550 participants with post-baseline safety data, 318 (57.8%) achieved treatment success; 54.4% of those within the first 8 weeks. A post hoc analysis evaluated maintenance of effect in participants who were enrolled ≥8 weeks and achieved clear during the study (n=56). Of these participants: 28.6% did not require any HP/TAZ retreatment after first achievement of clear, 53.6% did not require retreatment for ≥85 days, 62.5% for ≥57 days, and 83.9% for ≥29 days.

Conclusions: Though the study design was limited by requiring individuals to stop using HP/TAZ lotion at the time of first treatment success, many patients achieved clear skin, half of whom did not require retreatment for at least 3 months. These data indicate a relatively long maintenance of therapeutic effect with HP 0.01%/TAZ 0.045% lotion.

Funding: Ortho Dermatologics

A New Tazarotene 0.045% Lotion Formulation for Moderate-to-Severe Acne: Efficacy And Safety in Phase 2 and Phase 3 Clinical Trials

Emil A Tanghetti[1]; William Philip Werschler[2]; Edward Lain[3]; Ashlie M Caronia[4]; Eric Guenin[5]; Susan Harris[6]; Anya Loncaric[6]; Radhakrishnan Pillai[6]

[1]Center for Dermatology and Laser Surgery, Sacramento, CA; [2]University of Washington, School of Medicine, Seattle, WA; [3]Austin Institute for Clinical Research, Austin, TX; [4]Premier Clinical Research, Spokane , WA; [5]Ortho Dermatologics, Bridgewater, NJ; [6]Bausch Health US, LLC*, Petaluma, CA*

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

Introduction: Current gel, foam, and cream tazarotene (TAZ) 0.1% formulations for acne can cause irritation. A new, lower-dose tazarotene 0.045% lotion formulation was developed utilizing polymeric emulsion technology, resulting in a uniform distribution of the active ingredient and hydrating excipients. Efficacy and safety were evaluated in one phase 2 and two phase 3 double-blind, vehicle-controlled, 12-week studies in participants with moderate-to-severe acne.

Methods: In the phase 2 study, participants aged ≥12 years (N=210) were randomized (2:2:1:1) to TAZ 0.045% lotion, TAZ 0.1% cream, lotion vehicle, or cream vehicle. In the two pooled phase 3 studies, eligible participants (aged ≥9 years; N=1,614) were randomized (1:1) to TAZ 0.045% lotion or vehicle lotion. Inflammatory and noninflammatory lesion count reductions and treatment success (percent participants achieving ≥2-grade reduction in Evaluator's Global Severity Scores and a clear/almost clear score) were evaluated. Treatment-emergent adverse events (TEAEs) were also assessed. For this analysis, phase 2 results from the cream and lotion

vehicles were combined.

Results: At week 12, TAZ 0.045% lotion was statistically superior to vehicle in the reduction from baseline in inflammatory lesions (ph2: 63.8% vs 51.4%; pooled ph3: 57.9% vs 47.8%; P<0.01 both) and noninflammatory lesions (ph2: 56.9% vs 35.2%; pooled ph3: 56.0% vs 42.0%; P<0.001 both). Additionally, TAZ 0.045% lotion was as effective as TAZ 0.1% cream in reducing inflammatory/noninflammatory lesion counts in the phase 2 study. A greater percentage of TAZ 0.045%-treated participants achieved treatment success versus vehicle across all studies, though this difference did not reach statistical significance in the phase 2 study (ph2: 18.8% vs 10.1%; pooled ph3: 30.4% vs 17.9%; P<0.001). TEAE rates for TAZ 0.045% were 14.7% (ph2) and 26.8% (pooled ph3) versus vehicle (13.4% and 19.1%, respectively). Fewer TEAEs were reported for TAZ 0.045% lotion vs TAZ 0.1% cream (14.7% vs 26.8%). Mean cutaneous safety/tolerability scores at week 12 across all studies were <0.5 (1=mild) following treatment with TAZ 0.045% lotion.

Conclusions: In a phase 2 and two pooled phase 3 studies, lower-dose TAZ 0.045% lotion was more effective versus vehicle in the treatment of moderate-to-severe acne. In the phase 2 study, TAZ 0.045% lotion had fewer TEAEs than TAZ 0.01% cream. Overall, this new lotion formulation is a viable treatment option that is effective and has fewer TEAEs than TAZ 0.01% cream.

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Trifarotene 50 µg/g Cream: An Effective and Safe Treatment for Moderate Facial and Truncal Acne

James Del Rosso, MD[1]; Jerry Tan, MD[2]; Jonathan Weiss, MD[3]; Linda Stein Gold, MD[4]; Fran Cook-Bolden, MD[5]; Lawrence Eichenfield, MD[6]; Emil Tanghetti, MD[7]; Michael Graeber, MD[8]; Alessandra Alió Saenz, MD[8]; Faiz Ahmad, PhD[8]

[1]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV; [2]Windsor Clinical Research Inc, Windsor, Ontario, Canada; [3]Gwinnett Dermatology Clinical Research Center, Snellville, GA; [4]Department of Dermatology, Henry Ford Hospital, Detroit, MI; [5]Skin Specialty Dermatology, New York, NY; [6]Departments of Dermatology and Pediatrics, University of California San Diego, School of Medicine and Rady Children's Hospital, San Diego, CA; [7]Center for Dermatology & Laser Surgery, Sacramento, CA, [8]Galderma R&D, Fort Worth, TX

Introduction: While ~50% of patients with facial acne have truncal acne, data concerning treatment of truncal acne has been lacking. Three recent studies evaluated the efficacy and safety of a new retinoid, trifarotene 50 ug/g cream (trifarotene), for facial and truncal acne.

Methods: Two multi-center, randomized, double-blind, vehicle controlled, 12-week Phase 3 studies ("Perfect" 1+2) and 1 multi-center, open-label, non-comparative 52-week study ("Satisfy") investigated trifarotene once-daily in moderate facial and truncal acne. Efficacy endpoints included the Investigator's Global Assessment (IGA 0-4, face), the Physician Global Assessment (PGA 0-4, trunk), and the change in facial/truncal inflammatory and non-inflammatory lesions. Safety assessments included adverse events and local tolerance (erythema, scaling, dryness and stinging/burning).

Results: The "Perfect" studies recruited 2420 subjects, and 1214 were treated with trifarotene. "Satisfy" enrolled 455 subjects and 348 (76.5%) completed the 52-week study. All three studies met all efficacy endpoints, and both IGA and PGA successes (score 0-1, and 2-grade improvement) continued to increase throughout the full 52 weeks of the "Satisfy" study. There was a 29.4% IGA success rate with trifarotene compared with 19.5% for vehicle in "Perfect 1," and 42.3% trifarotene IGA success rate compared with 25.7% for vehicle in "Perfect 2." Signs/symptoms of local tolerability were mostly mild/moderate. Local irritation increased during week 1 on the face, up to week 2-4 on the trunk, decreasing thereafter, and was managed with moisturizers and/or regimen (application frequency) adjustment.

Summary: Trifarotene was effective and safe in 3 Phase 3 studies of moderate facial and truncal acne.

Integrated Safety Results of Two Phase-3 Trials of Guselkumab in Patients with Psoriatic Arthritis Through the Placebo-Controlled Periods

Proton Rahman[1], Christopher Ritchlin[2], Philip Helliwell[3], Wolf-Henning Boehncke[4], Philip Mease[5], Alice B Gottlieb[6], Shelly Kafka7, Alexa Kollmeier[8], Elizabeth Hsia[8,9], Xie L Xu7, May Shawi[7], Shihong Sheng[8], Prasheen Agarwal[8], Bei Zhou[8], Paraneedharan Ramachandran[8], Iain McInnes[10]

[1]Memorial U Newfoundland, St. Johns, Canada; [2]U Rochester, Rochester, USA; [3]U Leeds, Leeds, UK; [4]Geneva U Hospitals, Geneva, Switzerland; [5]Swed Med Ctr/Providence St Joseph Health and U Wash School of Med, Seattle, USA; [6]Icahn Med School/ Mt Sinai, NY, USA; [7]Janssen Scientific Affairs, Horsham, USA; [8]Janssen Research & Development, LLC, Spring House, USA; [9]U PA Med Ctr, Phila, USA; [10]U Glasgow, Glasgow, UK

Background: DISCOVER-1 &-2, are phase-3 psoriatic arthritis (PsA) trials investigating guselkumab, an IL-23p19 subunit-inhibitor. In both studies, guselkumab showed significant improvement versus placebo through week-24 in the placebo-controlled period.[1,2] The study was aimed to present integrated safety results of DISCOVER-1 &-2 through the placebo-controlled periods.

Methods: Adult with active PsA despite standard-therapy were enrolled. All patients were biologic-naïve, except~30% in DISC-1 with previous exposure to 1-2 TNF-inhibitors. Patients were randomized to SC guselkumab-100 mg Q4W; guselkumab 100 mg at W0, W4, then Q8W; or placebo. Adverse-events (AEs) and lab-results were analyzed from pooled data.

Results: The rates of patients experiencing ≥1 AE (Q4W, n=182; Q8W, n=182; Placebo n=176), serious-AE (Q4W n=8; Q8W n=7; Placebo n=12), infection (Q4W n=80; Q8W n=73; Q8W n=77), serious infection (Q4W n=3; Q8W n=1; Placebo n=3), and discontinuation due to an AE (Q4W n=8; Q8W n=5; Placebo n=7) were similar between guselkumab and placebo. There were 2 deaths, 3 malignancies, 2 Major Adverse Cardiac Events (MACE), and no opportunistic infections (treatment group not shown to prevent unblinding). Among the AEs reported

by ≥5% patients in any group, nasopharyngitis (Q4W, n=19; Q8W, n=26; Placebo, n=17) and elevated serum hepatic aminotransferases were more common with guselkumab versus placebo. Laboratory ALT and AST elevations were mostly mild, transient, and not associated with significant bilirubin elevation. There was a trend to decreased neutrophil count (mostly Grade 1, transient, and not associated with infection) with guselkumab versus placebo. Low rates of injection-site reactions (Q4W, n=4; Q8W, n=5; Placebo, n=1) were seen with guselkumab versus placebo. Anti-guselkumab antibody development was also low (Q4W, n/N=9/371; Q8W, n/N=6/373).

Conclusions: Guselkumab was safe and well-tolerated through the placebo-controlled period in 2 randomized, phase-3 trials of patients with active PsA. There were no meaningful safety differences between the Q8W and Q4W groups, no significant safety issues identified when comparing guselkumab to placebo, and no safety-signals with regards to infections, malignancy, and MACE. The safety profile of guselkumab Q4W and Q8W in PsA patients was generally consistent with that in the phase-3 trials of guselkumab Q8W for psoriasis.[3,4]

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Efficacy and Safety of Guselkumab, a Monoclonal Antibody Specific to the p19-Subunit of Interleukin-23, Through Week 52 of a Phase 3, Randomized, Double-blind, Placebo-controlled Study Conducted in Biologic-naïve Patients with Active Psoriatic Arthritis

Iain B. McInnes[1], Proton Rahman[2], Alice B. Gottlieb[3], Elizabeth C. Hsia[4,5], Alexa P. Kollmeier[4], Xie L. Xu[4], Ramanand A. Subramanian[4], Prasheen Agarwal[4], Shihong Sheng[4], Yusang Jiang[4], Bei Zhou[4], Désirée van der Heijde[6], Philip J. Mease[7]

[1]U Glasgow, Glasgow, UK; [2]Memorial Univ Newfoundland, St. Johns, NL, Canada; [3]Icahn School Med Mt Sinai, NY, NY, USA; [4]Janssen Research & Development, LLC, Spring House, PA, USA; [5]U Penn Med Ctr, Phila, PA, USA; [6]Leiden Univ Med Ctr, Leiden, The Netherlands; [7]Swedish Med Ctr/Providence St Joseph Health, U Washington, Seattle, WA, USA

Background: Guselkumab (GUS), a monoclonal antibody that specifically binds to the p19-subunit of IL-23, is approved to treat psoriasis. Through Week24 (W24) of the Ph3, double-blind, placebo (PBO)-controlled trial in biologic-naïve pts with active PsA (DISCOVER-2), GUS every 4/8 weeks (Q4W/Q8W) demonstrated efficacy for joint & skin symptoms and inhibition of structural damage progression (Q4W), and was well-tolerated. Objective is to assess GUS efficacy and safety through W52.

Methods: Biologic-naïve adults with active PsA (≥5 swollen+≥5 tender joints; CRP ≥0.6mg/dL) were randomized (1:1:1) to GUS 100mg Q4W; GUS 100mg at W0, W4, Q8W; or PBO. At W24, PBO pts switched to GUS 100mg Q4W (PBOXQ4W). ACR response rates at W52, based on nonresponder imputation (NRI) for missing data and as observed in pts who continued study agent at W24, are shown. Observed data for additional endpoints, including PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52 (or at d/c) and scored in a new Read Campaign, are shown.

Results: 712/739 (96.3%) randomized & treated pts continued study agent at W24; 689/739 (93.2%) completed Wk52. NRI ACR20 response rates continued to increase after W24, and at W52 were 70.6% for GUS Q4W and 74.6% for GUS Q8W. Similar response patterns were observed for the more stringent ACR50/70 criteria. Observed ACR, IGA, PASI & MDA/VLDA responses; dactylitis & enthesitis resolution; mean improvements in HAQ-DI and SF-36 PCS/MCS scores were also sustained through W52 in pts receiving Q4W & Q8W; W52 data for PBOXQ4W pts were generally consistent with other GUS-treated pts. Changes in vdH-S scores were similar for W24-52 (0.62) and W0-24 (0.46) for Q4W; less radiographic progression occurred from W24-52 v W0-24 for Q8W (0.23 v 0.73) & PBO X Q4W (0.25 v 1.00). In 731 GUS-treated pts, 4.2% had SAEs; 1.2% had serious infections; no pt died; and no pt had IBD, opportunistic infections or active TB, or anaphylactic or serum sickness-like reactions.

Conclusion: In biologic-naïve pts with active PsA, GUS elicited sustained improvements in joint & skin symptoms; inhibition of radiographic progression & improvements in physical function, quality of life & composite indices through W52. GUS safety in PsA was similar at W24[1] & W52 and consistent with GUS safety in psoriasis.

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Integrated Safety and Efficacy Analysis of FMX103 1.5% Topical Minocycline Foam for the Treatment of Moderate-to-Severe Papulopustular Rosacea: Results From Two Phase 3 Studies

James Q. Del Rosso, DO[1], Linda Stein Gold, MD[2], Leon Kircik, MD[3], Neal D. Bhatia, MD[4], Neil Sadick, MD[5], Matthew Zirwas, MD[6], Edward Lain, MD[7], Iain Stuart, PhD[8]

[1]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV; [2]Henry Ford Health System, Detroit, MI; [3]Icahn School of Medicine, New York, NY; [4]Therapeutics Clinical Research, San Diego, CA; [5]Sadick Dermatology, New York, NY; [6]Sanova Dermatology, Austin, TX; [7]Dermatologists of the Central States, Columbus, OH; [8]Foamix Pharmaceuticals, Bridgewater, NJ

Background: FMX103 1.5% minocycline foam is a novel topical medication being developed for the treatment of moderate-to-severe papulopustular rosacea.

Methods: Integrated safety and efficacy analysis of two Phase 3, randomized, multicenter, double-blind, vehicle-controlled studies (FX2016-11, N=751, and FX2016-12, N=771) comparing FMX103 1.5% vs vehicle foam in the treatment of moderate-to-severe papulopustular rosacea. Subjects applied the assigned drug once daily for 12 weeks. Co-primary efficacy endpoints were the absolute change from baseline to week 12 in inflammatory lesions

and the proportion of subjects achieving Investigator Global Assessment (IGA) treatment success at week 12. Saftey endpoints included adverse events (AEs), physical exams, vital signs, laboratory tests, and local facial tolerability assessments.

Results: The integrated efficacy population consisted of 1522 subjects (FMX103 1.5%, n=1009; vehicle, n=513), predominantly female (70.6%), and ranging in age from 18-86 years. Overall for the pooled population, FMX103 1.5% demonstrated statistically significant advantages over vehicle foam for both the change from baseline to week 12 in inflammatory lesions (P<0.001) and the proportion of subjects achieving IGA treatment success at week 12 (P<0.001). This statistical advantage of FMX103 1.5% over vehicle foam was observed for both co-primary endpoints in sub-populations of subjects that had either moderate (IGA-3) or severe (IGA=4) baseline disease severity. Notably, the reduction from baseline to week 12 in inflammatory lesions was more pronounced in the severe subpopulation. Treatment-emergent AEs (TEAEs) were experienced by 22.4% of subjects, with the incidence balanced between treatment groups (FMX103, 21.7%; vehicle, 23.8%). The most frequently reported TEAEs, in the FMX103 1.5% and vehicle groups, respectively, were viral upper respiratory tract infection (2.4% vs 2.3%) and upper respiratory tract infection (1.9% vs 2.5%). Similar rates of mild, moderate, and severe TEAEs were observed across both treatment groups. Serious TEAEs occurred in 8 subjects (0.3% for FMX103 1.5%; 1.0%for vehicle); all were unrelated to treatment. TEAEs leading to drug withdrawal occurred in 9 subjects (0.7% for FMX103 1.5%; 0.4% for vehicle); only 1 was considered related (moderate pruritus, FMX103 1.5%). For the facial tolerability assessments at week 12, both groups had higher percentages of subjects reporting "none" vs baseline, and the assessments trended toward improving scores.

Conclusions: This pooled analysis demonstrated that FMX103 1.5% appears to be a safe and efficacious topical treatment option for the treatment of moderate-to-severe facial papulopustular rosacea.

Long-Term Safety of Risankizumab in Patients With Moderate-to-Severe Plaque Psoriasis: Results From Pooled Clinical Studies

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

[1]K Papp Clinical Research and Probity Medical Research, Waterloo, ON, Canada; [2]Medical College of Wisconsin, Milwaukee, WI, United States; [3]Saint-Louis Hôpital, Sorbonne Paris Cité University Paris Diderot, Paris, France; [4]Oregon Medical Research Center, Portland, OR, USA; [5]AbbVie Inc., North Chicago, IL, United States; [6]Center for Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, and Skinflammation® Center, Hamburg, Germany

Background: Risankizumab inhibits interleukin-23, a key regulatory cytokine involved in psoriasis pathogenesis. The objective of this pooled analysis of psoriasis clinical studies was to investigate the long-term safety of risankizumab.

Methods: Risankizumab safety was evaluated through week 16 (short-term) in data pooled from five phase 2–3 trials of risankizumab 150mg vs adalimumab, ustekinumab, and placebo, and long-term(17 trials, all-risankizumab population, data cutoff March 25, 2020). The occurrence of any adverse event (AE) was reported among patients who received at least one dose of risankizumab. Treatment-emergent AEs were defined as any event with an onset after the first dose of risankizumab and within 105 days (short-term) or 140 days (long-term) after the last dose of study drug in the analysis period. Data are reported as number of patients with AEs and events per 100 patient-years (PYs).

Results: AEs occurred in 48.9% (638/1306), 56.9% (173/304), 52.3% (125/239), and 48.3% (145/300) of patients receiving risankizumab 150 mg, adalimumab, ustekinumab, and placebo, respectively, through week 16; serious AEs occurred in 2.4%, 3.0%, 5.0%, and 4.0%. AEs were generally comparable across treatments and most were mild-to-moderate in severity. In the all-risankizumab population (3072 patients; 7927.2 PY; median treatment duration 2.9 years with 5.6% ≥4 years), AEs occurred in 2482 (80.8%) patients corresponding to 170.9 events/100 PY. Serious AEs remained consistent over short-term (9.9/100 PY) and long-term (7.8/100 PY) treatment. Infections (90.8/100 PY short-term and 56.4/100 PY long-term) and serious infections (1.7/100 PY short-term and 1.2/100 PY long-term) did not increase over time. The most common infections over the long term were nasopharyngitis (16.8/100 PY) and upper respiratory tract infection (9.1/100 PY), and serious infections were sepsis (0.2/100 PY) and pneumonia (0.1/100 PY). There were no cases of active tuberculosis. The rate of malignant tumors excluding non-melanoma skin cancer (NMSC) was 0.7/100 PY short-term and 0.5/100 PY long-term; no trend in the events was observed. The rate of NMSC was 0.7/100 PY over short- and long-term. The rate of adjudicated major adverse cardiovascular events was 0.2/100 PY short-term and 0.3/100 PY long-term.

Conclusions: This pooled analysis is the largest reporting of safety data for risankizumab to date, encompassing more than 3000 patients with over 7900 PY of exposure from the psoriasis clinical trial program. The findings show that risankizumab treatment is safe and well tolerated with long-term treatment (up to ≥4 years) in patients with moderate-to-severe psoriasis.

Ligelizumab as Add-On Therapy for Patients with H1-Antihistamine-Refractory Chronic Spontaneous Urticaria: Primary Results of a Placebo- and Active-Controlled Phase 2B Dose Finding Study

Maurer M[1], Giménez-Arnau A[2], Sussman G[3], Loeffler J[4], Barve A[5], Severin T[4], Janocha R[4]

[1]Department of Dermatology and Allergy, Charité - Universitätsmedizin Berlin, Germany, [2]Dermatology Department, Hospital del Mar-Parc de Salut Mar, Universitat Autònoma Barcelona, Spain. [3]Division of Allergy and Clinical

Immunology, University of Toronto, Canada, [4]Novartis Pharma AG, Basel, Switzerland, [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States

Introduction: Ligelizumab is a humanized monoclonal anti-IgE antibody that binds with stronger affinity to IgE than does omalizumab, which is currently the only licensed therapy available for patients with chronic spontaneous urticaria (CSU) who remain symptomatic despite standard of care. This phase 2b dose-finding study examined the efficacy and safety of ligelizumab in patients with CSU that is inadequately controlled with H1-antihistamines (H1-AH) alone or in combination with H2-AH and/or leukotriene receptor antagonists.

Method: Adult patients with moderate to severe CSU (Urticaria Activity Score [UAS7]≥16) were enrolled. Patients were randomized to receive subcutaneous ligelizumab 24 mg, 72 mg or 240 mg, omalizumab 300 mg, or placebo every 4 weeks over 20 weeks (5 administrations in each arm), or a single dose of ligelizumab 120 mg. The primary endpoint was complete hives response (Hives Severity Score [HSS7] =0) at Week 12. Other endpoints assessed were the percentage of patients with UAS7=0 and Dermatology Life Quality Index (DLQI) =0–1 at Weeks 4, 12, and 20.

Results:A total of 382 patients were included. The primary objective of the study was achieved, with ligelizumab demonstrating a dose-response relationship with respect to complete hives response rates at Week 12 (P<0.001). HSS7=0 response rates at Week 12 were 30%, 51%, and 42% for ligelizumab 24 mg, 72 mg, and 240 mg, respectively, vs 26% for omalizumab and 0% for placebo. These responses were maintained up to Week 20 (26%, 51%, and 45% for ligelizumab 24 mg, 72 mg, and 240 mg, respectively, vs 34% for omalizumab and 9% for placebo). High response rates (UAS7=0 and DLQI=0–1) were observed as early as Week 4; more patients were symptom free (UAS7=0) and reported marked improvement of their quality of life (DLQI=0–1) with ligelizumab 72 mg and 240 mg vs omalizumab throughout the 20 week treament period. Ligelizumab was well- tolerated and the safety profile was comparable to that of omalizumab.

Conclusion: In patients with moderate to severe CSU, ligelizumab exhibited a clear dose response in HSS7=0 at Week 12. Compared with omalizumab 300 mg, ligelizumab achieved higher efficacy across multiple endpoints and showed comparable safety.

Ligelizumab Achieves Rapid Onset of Action, Improved and Sustained Efficacy Compared with Omalizumab in Patients With Chronic Spontaneous Urticaria Not Adequately Controlled by H1-Antihistamines

Maurer M[1], Giménez-Arnau A[2], Sussman G[3], Loeffler J[4], Barve A[5], Hua E[6], Balp MM[4], Severin T[4], Janocha R[4]

[1]Department of Dermatology and Allergy, Charité - Universitätsmedizin Berlin, Germany, [2]Dermatology Department, Hospital del Mar-Parc de Salut Mar, Universitat Autònoma Barcelona, Spain. [3]Division of Allergy and Clinical Immunology, University of Toronto, Canada. [4]Novartis Pharma AG, Basel, Switzerland. [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States. [6]Shanghai Novartis Trading Ltd., Shanghai, China.

Introduction: Ligelizumab is a humanized monoclonal anti-IgE antibody that binds with stronger affinity to IgE than does omalizumab, currently the only therapy to treat chronic spontaneous urticaria (CSU) inadequately controlled by H1-antihistamines (H1-AH). This phase 2b study examined the efficacy and safety of ligelizumab in patients with CSU whose symptoms remain uncontrolled with H1-AH alone or in combination with H2-AH and/or leukotriene receptor antagonists.

Method: Eligible patients with moderate to severe CSU (Urticaria Activity Score [UAS7]≥16) were randomized to subcutaneous ligelizumab 24 mg, 72 mg, or 240 mg, omalizumab 300 mg, or placebo every 4 weeks (q4w) over 20 weeks. Following the treatment period, patients entered a 24-week treatment-free follow-up period. The primary endpoint was the proportion of patients achieving complete hives response (Hives Severity Score [HSS7]=0) at Week 12. Other endpoints included change from baseline (BL) in HSS7, Itch Severity Score (ISS7), Urticaria Activity Score (UAS7; HSS7+ISS7), and proportion of patients achieving ISS7=0 and UAS7=0.

Results: 382 patients were included. Ligelizumab demonstrated a dose-response relationship with respect to complete hives response rates at Week 12 (P<0.001). High complete response rates (UAS7=0) were observed starting at Week 4; more patients were symptom free with ligelizumab 72 mg and 240 mg vs omalizumab throughout the treatment period. At Week 20, UAS7=0 response rates were 18.6%, 39.3%, and 40.0% for ligelizumab 24 mg, 72 mg, and 240 mg, respectively, compared with 30.6% for omalizumab and 4.7% for placebo. The median time to loss of complete response was 10.5 weeks for ligelizumab 240 mg, 4 weeks each for ligelizumab 72 mg and omalizumab 300 mg, and 3 weeks for ligelizumab 24 mg.

Improved changes from BL in HSS7, ISS7, and UAS7 were observed with ligelizumab 72 mg and 240 mg vs omalizumab and ligelizumab 24 mg. At the end of the treatment period, mean changes from BL in UAS7 were -15.2, -23.1, and -22.5 for ligelizumab 24 mg, 72 mg, and 240 mg, respectively, -18.2 for omalizumab 300 mg, and -13.6 for placebo. Mean changes from BL in HSS7 and ISS7 followed similar trends as UAS7, with ligelizumab 72 mg and 240 mg exhibiting the greatest changes throughout the treatment period; the benefit in favor of these two ligelizumab doses was sustained up to Week 32.

Discussion: Ligelizumab 72 mg and 240 mg q4w exhibited earlier and greater improvements in clinical responses with all other treatment groups. Ligelizumab 240 mg demonstrated a more durable treatment effect than omalizumab.

Real World Patient Perceptions of the use of Tazarotene 0.1% Foam in the Treatment of Acne Vulgaris

James Q. Del Rosso DO FAOCD, FAAD[1]; Corey L. Hartman MD FAAD[2]; Caitlin Lewis PhD[3]; Rhonda Schreiber MSRN[4]

Introduction: Acne vulgaris (AV) is the most common

inflammatory skin disorder seen in outpatient dermatology clinics in the United States. Both adolescents and adults of all races and both genders are frequently affected. In addition to the impact of AV on physical appearance, there are several adverse psychosocial consequences that impair quality of life. Continued patient compliance with topical therapies is a recognized barrier to optimal treatment of chronic disorders such as AV. Patient satisfaction with a topical vehicle formulation strong influences adherence with treatment. Tazarotene 0.1% foam is the only retinoid approved for use in a foam vehicle and is well established as an effective, safe, and well tolerated topical treatment for AV. Data from the Phase III studies evaluating tazarotene 0.1% foam for AV supported positive patient experiences with both therapeutic outcomes and formulation characteristics. These overall positive patient experiences prompted a subsequent analysis using a series of surveys administered to current users of tazarotene 0.1% foam to gather perspectives on its use in "real world" clinical practice.

Methods: Patients with AV on the face and/or trunk who were being treated with tazarotene 0.1% foam were asked to rate their experiences using the product over the course of 12 weeks. Surveys were administered at weeks 2, 4, 8 and 12 to gather feedback on patient satisfaction with the product, perceived therapeutic impact on AV, skin tolerability, and topical vehicle preference. Patients completed surveys within 3 days to ensure feedback was gathered at the specific timepoints. Two waves of the survey were administered in order to capture use in the winter months as well as non-winter months.

Results: 372 patients participated through week 12. 71% of respondents were either satisfied or very satisfied with the product, with 67% indicating that they were likely or very likely to continue use and only 6% saying they were unlikely to continue use. At week 12 although satisfaction was rated as very favorable overall, the highest levels were reported by the following subsets: female patients, those who used the product on their face only, those who used the product in winter, and those who used the product most consistently.

Conclusions: The completed surveys represent a significant sample size of patients with diversity across gender, race, and age. Overall, these real-world responses support the results of patient questionnaires from the Phase III studies with tazarotene 0.1% foam, being rated by a strong majority of patients as an effective, tolerable, and easy-to-use treatment option for AV of the face and body.

Affiliations: 1. JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV; Touro University, Henderson, NV; 2. Skin Wellness Dermatology, Birmingham, AL; University of Alabama Birmingham, AL; 3. Clewy Communications, Raleigh, NC; 4. Mayne Pharma, Greenville, NC. These surveys and analysis were sponsored by Mayne Pharma.

Real World Patient Perceptions of the use of Calcipotriene Foam 0.005% in the treatment of Plaque Psoriasis

Francisco Kerdel MD, FAAD;[1] Christine Don PA, MCMSc;[2] Renata Block PA-C, MMS; Caitlin Lewis PhD;[3] Rhonda Schreiber MSRN[4]

Introduction: Psoriasis is a common chronic immune-mediated inflammatory disease of the skin, with approximately 150,000 newly diagnosed patients in the United States each year. Most patients report their disease has significant negative physical and psychosocial impacts on their lives. Historically topical psoriasis treatments have been associated with poor compliance, which negatively impacts treatment success and patient satisfaction. Patient perception of vehicle attributes have been shown to influence treatment adherence. Calcipotriene foam, 0.005% is the only steroid-free vitamin D3 analog approved for use in a foam vehicle. Following the positive patient perception data previously collected in phase III trials of the foam, a series of surveys was administered to current users of calcipotriene foam, 0.005% to gather real world patient perspectives on its use.

Study Design: Patients with plaque psoriasis who were being treated with calcipotriene foam, 0.005%, were asked to rate their experiences using the product over the course of 8 weeks. Surveys were administered at baseline and weeks 2, 4 and 8 to gather feedback on patient satisfaction with the product, perceived improvement in their psoriasis with use of the product, and topical vehicle preference. Patients completed surveys within 3 days to ensure feedback was gathered at the specific timepoints.

Results: 277 patients completed the final survey at week 8, with 76% either satisfied or very satisfied with the improvement in psoriasis they saw with the product. At week 8 the highest satisfaction rates were reported by the following subsets: those using calcipotriene foam, 0.005% on the scalp alone (85%), those with severe psoriasis (>11% BSA) (80%), those using the those using the product as monotherapy (79%), followed closely by those using the foam on the scalp and body (78%). Satisfaction by gender was a negligible difference (76% males and 75% females) and no trend was seen across age groups (between 72-81%). Additionally, after using the foam for 8 weeks, 73% of participants indicated they were likely or very likely to continue use of the product.

Conclusions: The completed surveys represent a significant sample size of patients with diversity across gender, race and age. Calcipotriene foam, 0.005% has been rated by a strong majority of patients to be an effective and well tolerated treatment option, with low treatment fatigue and a high likelihood for compliance, supporting the results from the patient questionnaires in the Phase III clinical trials.

Affiliations: 1. Dermatology Residency Program at the LECOMT/Larkin Community Hospital, Palm Springs Campus, Hialeah, Florida; Florida Academic Dermatology Center, Coral Gables, Florida; Florida International University, Miami, Florida. 2. Florida Academic Dermatology Center, Coral Gables, Florida; 3. Clewy Communications, Raleigh, NC; 4. Mayne Pharma, Greenville, NC. These surveys and analysis were supported by Mayne Pharma.

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