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A Report from the 2024 American Academy of Dermatology Annual Meeting (AAD)

Lucas Galimany, MSc, MD, 2022 IPC Fellow

SUMMARIZING SESSIONS WITH A FOCUS ON PSORIASIS
The American Academy of Dermatology (AAD) held its 2024 Annual Meeting in San Diego, California, from March 8-12, 2024. The International Psoriasis Council (IPC) Symposium: The Comprehensive Care of Psoriasis covered hot topics such as obesity, anxiety, depression, cardiovascular risk, and other comorbidities. This congress report includes a summary of the IPC symposium presentations and other crucial psoriasis sessions throughout the conference.

**TABLE OF CONTENTS**

<table>
<thead>
<tr>
<th>IPC Symposium – The Comprehensive Care of Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>10</td>
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<tr>
<td></td>
</tr>
<tr>
<td>11</td>
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<td></td>
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<tr>
<td>13</td>
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<tr>
<td></td>
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<tr>
<td>15</td>
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<td>16</td>
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<tr>
<td></td>
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<tr>
<td>18</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>19</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other AAD Sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>21</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>23</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>25</td>
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<tr>
<td></td>
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<tr>
<td>26</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>28</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
### TABLE OF CONTENTS

#### Other AAD Sessions

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>Debate II: Oral Versus Biologic Therapy for the Treatment of Mild to Moderate Psoriasis</td>
<td>Kristina Callis Duffin, MD, MS, IPC Councilor</td>
</tr>
<tr>
<td>33</td>
<td>Late-Breaking Research - Session 1: High Induction Dosing of Risankizumab in Patients with Moderate-to-Severe Plaque Psoriasis: 52-week Results from Phase 2 KNOCKOUT Study</td>
<td>Andrew Blauvelt, MD, MBA, IPC Board Member</td>
</tr>
<tr>
<td>34</td>
<td>Late-Breaking Research - Session 1: The Light Treatment Effectiveness (LITE) Study: A Pragmatic Trial of Home vs Office Based Narrowband UVB Phototherapy for the Treatment of Psoriasis in the US</td>
<td>Joel Gelfand, MD, MSCE, IPC Board Member</td>
</tr>
<tr>
<td>35</td>
<td>Late-Breaking Research - Session 1: Efficacy and Safety of ESK-001, a Highly Selective Oral TYK2 Inhibitor, in a Phase 2 Study in Adults with Moderate-to-Severe Plaque Psoriasis (STRIDE)</td>
<td>Kim Papp MD, PhD, FRCP</td>
</tr>
<tr>
<td>36</td>
<td>Late-Breaking Research - Session 1: A Phase 2b, Long-Term Extension, Dose-Ranging Study of Oral JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis: FRONTIER 2</td>
<td>Laura Ferris, MD, PhD</td>
</tr>
<tr>
<td>37</td>
<td>Late-Breaking Research - Session 1: Efficacy and Safety of Apremilast for the Treatment of Japanese Patients with Palmoplantar Pustulosis: 16-week Results from a Phase 3, Randomized, Placebo-Controlled Trial</td>
<td>Tadashi Teuri, MD, PhD</td>
</tr>
<tr>
<td>39</td>
<td>Late-Breaking Research - Session 1: Bimekizumab Efficacy from Treatment Initiation Through 4 Years in Patients with Plaque Psoriasis: A Comprehensive, Long-Term, Pooled Analysis from BE BRIGHT</td>
<td>Mark Lebwohl, MD, IPC Councilor</td>
</tr>
<tr>
<td>40</td>
<td>Late-Breaking Research - Session 1: Guselkumab Showed Good Efficacy in Treating Generalized Pustular Psoriasis with Low Relapse Rate and Reduction in CD8+ Tissue Resident Memory T Cells</td>
<td>Yuling Shi, MD PhD (on behalf of Jiajing Lu, MD, PhD), IPC Councilor</td>
</tr>
<tr>
<td>41</td>
<td>The Translational Revolution in Inflammatory Skin Diseases</td>
<td>Mark Lebwohl, MD, IPC Councilor</td>
</tr>
<tr>
<td>42</td>
<td>Psoriasis: A Model Disease for Therapeutic Targeting</td>
<td>Bruce Strober, MD, PhD, IPC Board Member</td>
</tr>
<tr>
<td>44</td>
<td>Update on Pipeline Therapies for Psoriasis</td>
<td>Bruce Strober, MD, PhD, IPC Board Member</td>
</tr>
<tr>
<td>48</td>
<td>Impact on Comorbidities for Biologic Selection for Psoriasis</td>
<td>Jeffrey Marcus Cohen, MD</td>
</tr>
<tr>
<td>50</td>
<td>Clinical Considerations in Managing Women with Psoriasis</td>
<td>Jennifer Soung, MD</td>
</tr>
<tr>
<td>51</td>
<td>Comparative Efficacy and Relative Ranking of Psoriasis Biologics with Real-World and Clinical Trial Data</td>
<td>Mona Shahriari, MD</td>
</tr>
<tr>
<td>53</td>
<td>Translating AAD/NPF Guidelines to Your Clinical Practice to Lower Cardiovascular Risk in Patients with Psoriasis</td>
<td>Joel Gelfand, MD, MSCE, IPC Board Member</td>
</tr>
<tr>
<td>55</td>
<td>Treating Psoriasis while Preventing Psoriatic Arthritis: What are the Early Data?</td>
<td>Kenneth Gordan, MD, IPC Councilor</td>
</tr>
<tr>
<td>57</td>
<td>New and Emerging Biologics</td>
<td>Kenneth Gordan, MD, IPC Councilor</td>
</tr>
<tr>
<td>58</td>
<td>Psoriasis Comorbidities</td>
<td>Julia-Tatjana Maul, MD, IPC Councilor</td>
</tr>
</tbody>
</table>
Impact of Obesity on Psoriasis
Álvaro González-Cantero, MD, PhD, IPC Councilor
Hospital Ramón y Cajal University Hospital, Madrid, Spain

There has been an increasing incremental obesity trend over the last few years. About 42.4% of the US population has a body mass index of over 30, with morbimortality risks.\(^1\) Data from Spain also has noted that the prevalence of psoriasis patients who are overweight is double that of the control population.\(^2\)

Alvaro Gonzalez-Cantero, MD, shared that there is an inflammatory crosstalk in psoriasis comorbidities, and even if patients perform well with biologics from a “cutaneous” point of view, there are other problems that could not be controlled yet as subclinical inflammation.\(^3\)

A possible solution is that weight loss may improve psoriasis outcomes, accomplished by a low-dose diet, exercise programs, or bariatric surgery. A study showed that patients who lost 5% of their weight improved up to 26% of the psoriasis.\(^4\)

In this era of new oral and injectable treatments for obesity, there are even more options for our patients, including the potential role of glucagon-like peptide-1 (GLP-1) agonists in treating obesity in patients with immune-mediated diseases.\(^5\) In a randomized clinical trial with psoriatic and diabetes type-2 patients, using a GLP-1 agonist (Liraglutide) was associated with improved PASI scores.\(^6\) He remarked there is potential in using weight control drugs in patients that do not improve as we expect with systemics such as biologics.

In response to the question, “Is there an anti-inflammatory diet?” Dr. Gonzalez-Cantero showed some articles that support weight-reduction benefits in psoriasis.\(^7,8\)

References

Challenging Case: A Patient with Comorbid Solid Organ Malignancy

Maria-Angeliki Gkini, MD, MSc, PhD, FRCP, 2023 IPC Fellow
Barts Health NHS Trust, London, United Kingdom

Maria Angeliki Gkini, MD, MSc, PhD, FRCP, presented a case of a male patient with severe psoriasis and psoriatic arthritis who was treated with Secukinumab with an initial complete skin response. While on treatment, the patient developed anemia and bloody stools due to an ascending colon tumor that resulted in a moderately differentiated colon adenocarcinoma. Dr. Gkini showed data on the slightly increased risk of cancer among psoriasis patients, but treating them with biologics was not commonly associated with increased risks.¹ The joint AAD-NPF guidelines of care of psoriasis and comorbidities² state that psoriatic patients seem to have an increased incidence of lymphohematopoietic cancers, head and neck cancers, and digestive tract malignancies. Nevertheless, monoclonal antibody therapies (e.g., IL12/23, IL17, IL23) do not appear to alter malignancy risk.

The patient later had a recurrence of severe psoriasis in his skin and had swollen and painful joints. The British Association of Dermatologists guidelines for biologic therapy in psoriasis³ recommends discussing the risks and benefits of continuing versus stopping therapy in patients who developed or have completed recent cancer treatments. Dr. Gkini advised that each situation should be tailored on a case-by-case basis. According to other guidelines,⁴⁵⁶ the cancer prognosis is unlikely to be altered (low risk of recurrence or progression) by systemic psoriasis treatments in those patients with previous solid malignancy and good prognosis. The patient was restarted on Secukinumab with secondary failure and later switched to Guselkumab with PASI100 response. Dr. Gkini finally remarked on the importance of a multidisciplinary approach with informed patient and family decisions.

References
Identification and Management of Anxiety, Depression, and Stigma in Patients with Psoriasis

Evan Rieder, MD
Private Practice, New York, New York, United States

Patients with psychopathology are generally under-observed by dermatologists, which can translate to poor patient experience. Elevated rates of depression and anxiety, together with psoriasis, can lower quality of life (QoL) scores. Furthermore, suicidality and psoriasis have not been consistently associated, and the severity of psoriasis does not necessarily correlate with emotional toll.

Evan Rieder, MD, emphasized the psychological burden of psoriasis patients and the stigmatization that could derive from this condition. For years, there have been misconceptions about contagiousness or hygiene problems. All those factors may somehow represent the basis of social rejection, social anxiety, and even avoidant personality traits. A publication by Schut et al. showed that psoriasis patients had six times the increased risk of having body dysmorphic disorder.

To better identify these patients in the clinic, Dr. Rieder focused on the most relevant signs of subjects, including poor eye contact, slow movements, slow speech, poor posture, appearing to be on edge, being worrisome, hyper-fixation, perseveration, and obsession about minutiae.

Dr. Rieder recommended screening tools such as PHQ-2, GAD-2, and BDDQ-DV. For treatment options, Dr. Rieder suggested that personalized approaches are needed regarding psychopharmacology, psychotherapy, psychoeducation, and self-help. For patients taking selective serotonin receptor inhibitors, it takes about four to six weeks for the effect to be evident. Some other important tips for dermatologists and patients prescribed selective serotonin receptor inhibitors are to start with a low dose, be patient, and increase the dose every two weeks, depending on tolerability. After six weeks of intolerance, dermatologists can consider switching the prescription, or if there is a partial response, there are options to increase the dose. Ultimately, Dr. Rieder emphasized that combining different approaches (e.g., drugs, psychotherapy, self-care) is probably the best for these patients.

References

Challenging Case: A Patient with Infection
Lucas Galimany, MD, MSc, 2022 IPC Fellow
Pontificia Universidad Catolica de Chile, Santiago, Chile

Lucas Galimany, MD, MSc, presented a case of a 25-year-old male with a longstanding history of severe plaque psoriasis. This patient started on oral Methotrexate with PASI75 response at three months. After one year of treatment, he developed an abrupt onset of left occipital headache that rapidly evolved to holocranial severe pain associated with feverish feeling, photophobia, phonophobia, nausea, and vomiting. The neurologic examination and head and neck CT scan were unremarkable. Finally, lumbar puncture was performed, and cerebrospinal fluid showed high leukocyte and protein counts. An infectious panel with PCR resulted in a positive varicella-zoster virus (VZV) result. This patient was diagnosed with VZV meningitis, and intravenous Acyclovir was initiated. The patient recovered completely, but soon after discharge, he developed Ramsay Hunt syndrome and was re-admitted for another course of IV treatment with Acyclovir with good clinical response. Dr. Galimany reviewed the risk factors for herpes zoster, including 1) age (> 50 years), 2) immunosuppression states, 3) infection, and 4) mental stress. Data from Danish registries showed that the cumulative incidence of alpha-herpes virus infections increased, especially among psoriatic patients treated with anti-TNF alpha and Methotrexate. In a recent systematic review, JAK inhibition and zoster infections were analyzed from adult patients with psoriasis treated with JAK inhibitors. Deucravacitinib showed no statistical difference from placebo, and Tofacitinib showed increased odds of infection versus placebo (OR: 3.77). Finally, Dr. Galimany showed recommendations for the Shingrix vaccine in all patients older than 50 years and those under 50 years on JAK inhibitors, systemic steroids, or combinations of systemics.

References
Emerging Mechanistic Data Behind Psoriasis and Cardiometabolic Disease
Johann Gudjonsson, MD, PhD, IPC Board Member
University of Michigan, Department of Dermatology, Ann Arbor, Michigan, United States

Johann Gudjonsson, MD, PhD, began his presentation focused on psoriasis as a systemic inflammatory disorder with multiple comorbidities.\(^1\,\text{2}\) Studies have shown the association between psoriasis and cardiovascular disease, and some even show higher relative risks of myocardial infarction at younger ages.\(^3\)

Patients with improved PASI scores have shown improved blood pressure control, decreased systemic inflammation, and decreased coronary plaque burden.\(^4\) A recent study revealed a causal relationship between coronary artery disease and psoriasis, showing that inflammation involved in subclinical atherosclerosis may have a causal effect on psoriasis.\(^5\)

The same publication identified some common genes between both diseases (i.e., IL17A, IL6, NFKB1, TNF). There has been an associated increase of IL-17A in atherosclerosis and psoriasis, and its blockade decreased the size of atherosclerotic plaques.\(^6\) Another example is IL-23, which activates Th17 production of IL-17 and macrophages and dendritic cells that secrete inflammatory cytokines such as TNF-alpha.\(^7\) Cathelicidin LL37 increases and is an inflammatory mediator in psoriasis. Its role has been shown in LDL uptake in macrophages and changes in the lipid metabolism genes that could finally lead to atherosclerosis.\(^8\)

A study also linked vascular endothelial cells with the inflammatory infiltration of the skin in psoriasis.\(^9\)

In final remarks, Dr. Gudjonsson said that the causal link between psoriasis and cardiovascular disease may not be as straightforward as we have believed. Other confounders may also play a role, and the direction of effects seems stronger from cardiovascular risk to psoriasis than vice versa. Nevertheless, there is evidence of a possible bidirectional effect.

References

How to Identify Cardiovascular Risk in People with Psoriasis
Joel Gelfand, MD, MSCE, IPC Board Member
University of Pennsylvania, Philadelphia, Pennsylvania, United States

Joel Gelfand, MD, MSCE, asked the audience, “Which drug has demonstrated improvement of major cardiovascular events (MACE) in a randomized controlled trial?” The answer to this question was Colchicine. He pointed out the increased scientific interest, in the last few years, towards the relation between psoriasis and cardiovascular disease. Dr. Gelfand showed data from the iHOPE study (Incident Health Outcomes and Psoriasis Events), a prospective population-based cohort demonstrating that the body surface area affected by psoriasis predicts death and diabetes.¹

In a recently published article from Sweden, PASI scores showed that there is an independent risk factor for cardiovascular events.² Dr. Gelfand referred to inflammation as an important predictor of MACE, cardiovascular, and all-cause mortality from a study of patients with or who have a high risk of atherosclerotic disease.³ Since this association, there has been notable interest in evaluating risk changes upon targeted biologic drugs and others in psoriasis patients. However, data from a meta-analysis of randomized controlled trials have not demonstrated any significant effects until now.⁴ Dr. Gelfand presented data from a network meta-analysis that showed a negative effect of some biologics and TNF inhibitors correlated with a possible increased risk of MACE in patients with immune-mediated inflammatory disorders.⁵ Some data suggested that TNF-alpha inhibitors were likely cardioprotective but still inconclusive.⁶

Dr. Gelfand cited the 2019 American Association of Dermatology (AAD)/ the National Psoriasis Foundation (NPF) guidelines as a starting point for cardiovascular screening and risk management of psoriasis patients.⁷ As such, Dr. Gelfand recommends that arterial hypertension, diabetes mellitus, and hyperlipidemia should be assessed among all patients. Cardiovascular risk assessment should be performed, especially in patients between 40 and 75 years. Dr. Gelfand also showed the American College of Cardiology (ACC)/ American Heart Association (AHA) statin recommendations in which psoriasis is a risk enhancer that could determine initiation of moderate-intensity statin therapy for patients with borderline 10-year-cardiovascular risk.⁸ Finally, Dr. Gelfand highlighted the importance of working closely with preventative cardiology to better care for psoriasis patients.

References


There are different clinical presentations of psoriatic arthritis (PsA): peripheral arthritis, enthesitis, dactylitis, and spondylarthritis. It has been associated with uveitis, inflammatory bowel disease (IBD), and nail disease. The mean time from the beginning of psoriasis to the development or diagnosis of psoriatic arthropathy is about eight to ten years.

PsA develops after a combination of diverse factors such as genomics, metabolomics, proteomics, microbiome, and epigenome. Arthur Kavanaugh, MD, showed that DNA methylation changes may predict the development of PsA from psoriasis.¹

One of the dilemmas lacking clear answers is the real effect of biologic immunotherapy for psoriasis and its capability to prevent articular manifestations. Dr. Kavanaugh mentioned recent and ongoing studies on this topic, such as the PAMPA and FOREMOST studies.²

Finally, Dr. Kavanaugh referred the treatment recommendations for PsA based on the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) 2021 guidelines.³ Future directions are aimed towards treatment optimization, early intervention, treat-to-target, combinations (biologics, phosphodiesterase-4 inhibitors, JAK inhibitors), tapering, and discontinuation of therapies.

References
Challenging Case: A Pregnant Patient
Sonia Chavez-Alvarez, MD, 2023 IPC Fellow
Hospital Universitario Dr. José Eleuterio Gonzalez – UANL, Monterrey, Nuevo León, Mexico

Sonia Chávez-Álvarez, MD, presented the case of a 27-year-old female with acrodermatitis continua of Hallopeau and genital psoriasis that was initially treated with topicals, with partial response. The patient was treated later with Guselkumab with an improvement of her lesions, and after 1.5 years, she wanted to explore the option of pregnancy and stop systemic treatment. Dr. Chávez-Álvarez reviewed approved topical treatments for pregnancy (tacrolimus and steroids) and those not recommended during pregnancy (calcipotriene, tazarotene, coal tar, PDE-4 inhibitors, tapinarof).¹,² Dr. Chávez-Álvarez showed data on the prognosis of psoriasis during pregnancy, in which 23% of women experience flares, and in about 55% of those cases, psoriasis improves.³,⁴

Some reported risks in pregnant psoriatic patients are increased gestational diabetes, cesarean delivery, (pre) eclampsia, pre-term birth, spontaneous abortions, and postpartum depression.⁴ Dr. Chávez-Álvarez showed that Certolizumab pegol is the only FDA-approved biologic during pregnancy, and most of the other biologics are category B (pregnancy) but should be avoided during the last trimester, with limited data.⁵ Studies looking for fetal risks on biologics have shown a similar prevalence of miscarriages and congenital malformations in the general population.⁶

The patient presented became pregnant and was treated during pregnancy with intralesional steroids. Dr. Chávez-Álvarez commented on UVB phototherapy as a treatment option for psoriasis in pregnancy, also remarking on the need for folic acid supplementation.¹,⁵ Finally, she discussed the risks of newborn infections of mothers who received biologics, with potentially altered immune response, if treatments are continued during the third trimester. She also advised against live vaccinations until the baby is at least six months old.⁶

References
Hot Psoriasis Topics: Single Cell RNA Sequencing
Andrew Blauvelt, MD, MBD, IPC Board Member
Blauvelt Consulting LLC, Lake Oswego, Oregon, United States

There continues to be a vast improvement in the development of single-cell RNA sequencing and the knowledge of pathogenesis in psoriasis. Dr. Blauvelt showed data from some recently published works.¹

Single-cell and spatial sequencing were used to define processes by which keratinocytes and fibroblasts amplify inflammatory responses in psoriasis. This study showed that IL-36 amplifies IL-17A responses in the supraspinous epidermis of psoriatic skin. Moreover, SFRP+ fibroblasts in psoriasis contributed to the immune response by transitioning from a pro-fibrotic to a pro-inflammatory state. These findings help to characterize cell types and cytokines that drive inflammation, including inflammatory fibroblasts.²

Fries et al. focused on analyzing gene expression dealing with major cell types in psoriatic lesions. This study combined single-cell RNA sequencing, TCR sequencing, and spatial transcriptomics to explain the role of IL-26, a Th17 cytokine with known pro-inflammatory functions. IL-26-producing cells were seen as an early differentiation state of Th17 cells that infiltrate psoriasis skin and induce TFG-β1 expression from keratinocytes that promote their differentiation into IL-17A-producing cells.³

This publication focused on the earliest cell and cytokine changes in psoriatic skin following initiating IL-23 inhibitors. In this study, single-cell RNA sequencing was performed at baseline, at three and 14 days following Risankizumab administration. Inflammatory fibroblast and myeloid population changes were the most extensive during the first weeks of treatment. The abundance of WNT5A+/IL24+ fibroblasts in psoriatic lesional skin was significantly reduced after treatment.⁴

In this study, single-cell RNA sequencing was done on serial skin biopsies in patients on an IL-23 inhibitor. The authors demonstrated a decline in IL-17-induced gene expression among IL23-inhibitor responders versus non-responders, with the persistence of T17 cells that continued driving the inflammation.

References
Bruce Strober, MD, PhD, presented data on new drugs for psoriasis patients. EFFISAYIL 1-2 studies were randomized controlled trials that used an IL-36 receptor antagonist (Spesolimab) to treat generalized pustular psoriasis.\textsuperscript{1,2} During flares, active treatment of Spesolimab achieved high rates of complete cure of pustulation after week one, and maintenance treatment with high-dose Spesolimab had an 84% risk reduction of developing flares.

Another new drug development (currently unapproved) is TAK-279, an oral presentation of a TYK-2 inhibitor. In the phase two study, 67% of patients achieved PASI75 response achieved after 12 weeks. Principal adverse effects were acne and acneiform reactions, with no severe safety issues.\textsuperscript{3}

The FRONTIER-1 study tested an oral peptide IL-23 receptor antagonist (first-in-class, oral, selective). This drug showed gastrointestinal stability and potency, and the 100 mg twice-daily dose showed the best efficacy, PASI 75 response in 78.6% of patients at week 16. No safety issues of relevance were observed.\textsuperscript{4}

Orismilast, a PDE4 inhibition drug (currently unapproved), rises as a new oral agent. The initial studies have shown good responses and tolerability, with PASI90 response in 24% of patients at week 16.\textsuperscript{5}

References
Andrew Blauvelt, MD, MBA, emphasized the importance of biomarkers as future tools to ideally guide discussions on prognosis and therapeutic choices moving towards precision medicine.\(^1\) This ultimate concept involves utilizing a series of analytical measures to determine the proper choice of therapy for patients. Dr. Blauvelt described two types of biomarkers of special interest in psoriasis: those related to “disease progression” (into severe skin disease or psoriatic arthritis) and those related to “drug response.” Two recent studies have been performed as scoping reviews on the utility of biomarkers in psoriasis regarding disease progression (genomic, proteomic, metabolic) and systemic treatment response (i.e., HLA C*06:02 positive patients respond better and faster to Ustekinumab versus HLA C*06:02 negative patients).\(^2\)\(^-\)\(^4\) There has also been recently published data on biomarkers for Secukinumab responses.\(^5\)

References

Evolving Landscape of Oral Therapies for Psoriasis

April Armstrong, MD, MPH, IPC Councilor
University of California Los Angeles, Los Angeles, California, United States

April Armstrong, MD, MPH, provides a robust evaluation of oral therapies in psoriasis. Apremilast is a well-known oral phosphodiesterase-4 inhibitor with FDA approval for plaque psoriasis regardless of disease severity. The ADVANCE study demonstrated that 21% of bio-naïve mild-moderate psoriasis patients achieved sPGA 0/1 at week 16.1

A novel PDE-4 inhibitor (ME3183) has been developed, and in-vitro analysis has shown a stronger inhibition of PD4B1 than marketed PDE4 inhibitors. Clinical studies have confirmed its efficacy with approximately 50% reduction of baseline PASI scores at week four. A greater proportion of patients on ME3183 active doses achieved PASI90 and sPGA 0/1 vs placebo. Safety analysis demonstrated more nausea, diarrhea, vomiting, headache, and lipase elevations.

The POETYK-1 study showed significantly higher sPGA 0/1 responses with the TYK-2 inhibitor (Deucravacitinib) versus Apremilast and placebo (week 24).2 The efficacy of these drugs has also been shown to be maintained after the three year follow-up. Nasopharyngitis and upper respiratory tract infections were among the most common adverse effects. Dr. Armstrong commented that Deucravacitinib could be an add-on drug for those patients with unmanageable moderate to severe psoriasis already on biologics. In the same line of TYK2 blockage, TAK-279 is a new oral drug in development. Its molecular conformation has shown high specificity for TYK-2 over JAK1-2-3. A phase 2b study confirmed the efficacy of this drug, with PASI75 and sPGA 0/1 at week 12 being present in a higher proportion of patients than the placebo group.4 The most frequent adverse events were COVID-19 infection, acne, or acneiform reactions. There were no laboratory abnormalities observed.

A new oral IL-23 receptor inhibitor is on the horizon, blocking IL-23 signaling.5 Initial studies have shown significant dose-response for PASI75/PAS90/PASI100 at week 16.6 It also demonstrated a favorable safety profile without clinically significant laboratory alterations from baseline.

In summary, new oral peptides and small molecules have evolved with similar inhibition targets as biologic drugs and more potent PDE4 inhibitors.

References
Nail Psoriasis or Onychomycosis? Pearls on Diagnosis and Management of Psoriatic Nail Disease
Boni Elewski, MD
University of Alabama at Birmingham, Birmingham, Alabama, United States

Boni Elewski introduced clinical presentations indicative of nail psoriasis and shared clues to aid diagnosis.\(^1,2\) First, it usually presents on fingernails (both hands) and is associated with a history of psoriasis or psoriatic arthritis. There could also be non-response to antifungals. Other typical clinical features of nail psoriasis include pitting, onycholysis with red borders, oil spots, or salmon-colored spots. On the other hand, onychomycosis most commonly affects the toenails, and tinea pedis is usually present. There is also a history of past tinea pedis and/or nails improving with oral antifungals.

Psoriasis could present only with nail involvement, but that should be around 5% of the patients. The nail psoriasis is present in up to 50% of patients with psoriasis and up to 90% of those with psoriatic arthritis.

Among clinical presentations of nail psoriasis, nail pitting is the most common feature, which is more irregular than in alopecia areata patients. We can also find onycholysis with red borders (more characteristic of psoriasis). Hyperkeratosis with onycholysis could also be psoriasis (distal subungual psoriasis) and like onychomycosis. However, splinter hemorrhages are not specific features.

The utilization of systemic treatment is recommended if there are four or more nails involved.\(^4\) If three or fewer nails are affected, topicals or systemic agents could be used. For nail psoriasis systemic treatment, meta-analyses have shown that Ixekizumab has the highest rate of nail clearance. In general, IL17 inhibitors have shown better efficacy outcomes at 24-27 weeks of follow-up (Ixekizumab, Brodalumab, Bimekizumab).\(^5,6\) At 48-52 weeks, the biologics that performed better for nail involvement were Ixekizumab, Adalimumab, and Brodalumab. Among IL23 inhibitors, Risankizumab and Guselkumab also show efficacy for this indication.

References
Debate I: Will Non-Steroidal Topical Medications Replace Topical Steroids in the Treatment of Psoriasis?
Kenneth Gordon, MD, IPC Councilor
Medical College of Wisconsin, Milwaukee, Wisconsin, United States

Bruce Strober, MD, PhD, IPC Board Member
Central Connecticut Dermatology, Cromwell, Connecticut, United States

Two viewpoints were presented: 1) non-steroidal topical medications will replace steroids, and 2) there is ongoing success of topical steroids.

Bruce Strober, MD, PhD, presented the viewpoint that non-steroidal topical medications will replace steroids. Dr. Strober stated that the options of non-steroidal topical products have been expanding through the last few years, and topical calcineurin inhibitors, phosphodiesterase-4 inhibitors, and aryl hydrocarbon receptor agonists are currently available.1-4 Several randomized controlled trials have demonstrated the efficacy of these new drugs, with good tolerability and no significant adverse effects. One advantage of changing to non-steroidal is that we can prescribe one medication that can be used indistinctively over different body surfaces (without fearing face or flexural areas). As access and cost improve for non-steroidal topicals and their generic equivalents appear, topical steroids will be relegated to secondary status.

Kenneth Gordon, MD, presented his talk as “The ongoing success of topical steroids.” He stated that there are so many options of steroids available, with different compounds and vehicles. Even new non-steroidal medications are prescribed in combination with steroids (such as betamethasone + calcipotriol) to enhance their potency. So far, in Dr. Gordon’s practice, topical steroids have been proven to have excellent efficacy, which aligns with the literature data. Regarding safety, there was no clinically significant HPA axis suppression, and the frequency of skin atrophy was low (between 0 and 5%). Topical steroids represent a highly effective, fast, safe, convenient, and affordable choice for our patients.

References
Mastering the Use of IL-23 Inhibitors in Psoriasis and Psoriatic Arthritis
Joel Gelfand, MD, MSCE, IPC Board Member
University of Pennsylvania, Philadelphia, Pennsylvania, United States

Joel Gelfand, MD, MSCE, reviewed psoriasis pathogenesis and the different therapeutic targeted drugs developed. Inflammatory myeloid dendritic cells produce both IL-12 and IL23 cytokines, and IL23 signaling determines Th17 cells differentiation for further IL17 signaling. Local IL-23 is required for the proliferation and retention of skin-resident memory Th17 cells. The IL23 inhibitors (IL23i) (Guselkumab, Tildrakizumab, Risankizumab) produce the blockage of this inflammatory pathway. If we examine the head-to-head trials of biologics for psoriasis, we can conclude that IL17i likely acts the fastest, but IL23i is likely the most effective at one-year follow-up. The ECLIPSE study showed a PASI 90 response at 48 weeks with Guselkumab (84%) and Secukinumab (70%). Data from the Cochrane Collaboration network meta-analysis on pharmacologic treatment for psoriasis showed the following IL23 inhibitors, Infliximab, Ixekizumab, Bimekizumab, and Risankizumab, were the most efficacious.

Dr. Gelfand said that based on Crohn’s disease studies of IL-23i, higher doses are given to inflammatory bowel disease (IBD) patients with good safety profiles. In a study by Dr. Blauvelt et al., they evaluated higher dosing regimens for psoriasis. At week 28, patients initially randomized to Risankizumab who achieved sPGA 0/1 were randomly assigned 1:2 to continue treatment or placebo. In the population that continued with placebo, the median time for relapse after stopping treatment was 210 days (IQR: 113-296) for loss of PASI90 response.

Data regarding the reduction of risk of developing psoriatic arthritis (PsA) in biologic treatment, unfortunately, is not yet clear. There is a lack of incident user designs, incomplete measurement of confounding variables, and selection and observation biases. Dr. Gelfand also commented on the risk of latent tuberculosis reactivation, as these drugs may not increase the risk despite the importance of IL-23 for INF gamma-dependent immunity in mycobacterial infections.

In summary, IL-23 inhibitors are among the highest efficacy biologics for psoriasis, with the longest treatment persistence, infrequent dosing, long duration of effect off-treatment, and well tolerated with no warnings for cancer, IBD, MS, CHF, and TB.

References


Practical Considerations in Using IL-17 Inhibitors for Psoriasis and Psoriatic Arthritis
Joseph Merola MD, MSc, IPC Councilor
Brigham and Women’s Hospital Harvard Medical School, Boston, Massachusetts, United States

There are well-suited scenarios to use IL-17 inhibitors (IL-17i), including patients that need rapid response, erythrodermic, severe forms, areas of special involvement, psoriatic arthritis, history of malignancy, tuberculosis, serious infection on other agents, and certain comorbidities (e.g., multiple sclerosis, severe congestive heart failure). There are four FDA-approved IL-17i agents for moderate to severe psoriasis.\(^1,2\) The advantage of IL-17i is that they treat all clinical domains of psoriatic arthritis (PsA) and have also shown an effect on radiographic progression.

In a network meta-analysis by Armstrong et al., IL-17i was among the most efficacious drugs to achieve PASI100.\(^3\) Following IL-17i were Ixekizumab, Brodalumab, and Secukinumab, respectively, in ranked order. Bimekizumab inhibition of IL-17 A/F has demonstrated long-term efficacy with maintenance of PASI90 response over 90% at 52 weeks. Ixekizumab has shown clinically significant responses in genital psoriasis (IXORA-Q study) based on sPGA0/1 responses at week 12. A phase four study by Papp et al. showed excellent responses at week 26 in patients with inadequate response to previous agents when switching to Brodalumab.\(^4\)

Joseph Merola, MD, MSc, also presented a study showing that Secukinumab dosing every two weeks was superior to every four weeks dosing in patients weighing 90 kg or more.\(^5\) Dr. Merola presented the BE-COMPLETE study data, including patients with active PsA and an inadequate response to TNFi in a phase three multicenter placebo-controlled randomized clinical trial.\(^6\) The primary endpoint (ACR50 response) was reached in 43.4% of patients with Bimekizumab 160 mg every four weeks versus 6.8% in the placebo group.

Sonelokimab, a newly developed IL-17 A/F nanobody, has been tested for PsA and has high response rates across all ACR levels. Another development has been intravenous Secukinumab, with weight-based dosing. Adverse events among IL-17i are generally mild (e.g., nasopharyngitis, upper respiratory infections, headache, tinea infections, and candidiasis). One main concern should be inflammatory bowel disease (IBD) among IL-17i users.

In summary, IL-17 inhibitors represent a very high-efficacy family of biologics with rapid onset of action across the breadth of psoriasis disease domains. There is already strong efficacy demonstrated for PsA (equivalent to Adalimumab), including prevention of radiographic progression.

References


Doppelgängers or Twins? What to Know About Biosimilars
Mark Lebwohl, MD, IPC Councilor
Icahn School of Medicine at Mount Sinai, New York, New York, United States

Mark Lebwohl, MD, defined the biosimilar concept in which no clinically meaningful differences in safety and efficacy form a “reference” biologic should be seen, and only minor variations in clinically inactive components are permitted.¹

Both biosimilars and their reference biologics share amino acid sequences and mechanisms of action.² Biosimilars are generally easier to develop, with a faster approval pathway. It should not have meaningful differences in safety, purity, and potency. To date, we have TNF alpha biosimilars and IL12/23 biosimilars. The FDA approved the IL12/23 biosimilar, but due to a lawsuit, the biosimilar’s launch will be delayed until 2025.

Dr. Lebwohl also presented data on interchangeability in psoriasis, which corresponds to switching to a biosimilar from its reference biologic without the prescriber’s consent.³ He also showed that incorporating TNF alpha biosimilars did not lower treatment costs. Mean quarterly insurer costs per patient were similar to the insurer cost for originator infliximab from 2017 and then moderately decreased in 2018.

References
Debate II: Oral Versus Biologic Therapy for the Treatment of Mild to Moderate Psoriasis
Kristina Callis Duffin, MD, MS, IPC Councilor
University of Utah Health Care, Salt Lake City, Utah, United States
Wilson Liao, MD, IPC Councilor
University of California San Francisco, San Francisco, California, United States

Wilson Liao, MD presented the evolution of “tried and true” semi-targeted therapies (e.g., methotrexate, acitretin, cyclosporine, fumarates) to the next generation “targeted” therapies (e.g., Apremilast, Deucravacitinib, oral IL12i (JNJ-2113), oral IL17i (DC-806)). Among current oral treatments, the only FDA-approved oral targeted treatment for mild psoriasis is Apremilast, based on the data on efficacy shown in the ADVANCE and PROMINENT studies. More recently, POETYK PSO1 and PSO2 studies have also shown high efficacy of oral selective TYK2 inhibition.\(^2,3\) In a subgroup analysis of both trials, Blauvelt et al. showed that in moderate patients, the sPGA 0/1 was achieved by 47.3% of subjects versus 9.2% in the placebo group. Dr. Liao also focused on the excellent safety profile of Apremilast without laboratory monitoring, together with its safety in cancer, HIV, and immunosuppressed patients. From the patient’s perspective, there has also been data on the preference for oral drugs over biologics. Some of the disadvantages that we can find with biologics are injection site reactions, possible anaphylaxis, loss of drug due to misfire, the requirement of refrigeration, the difficulty of traveling, and the hassle of disposal.\(^4\) Oral psoriasis drugs have proven efficacious, with superior to good safety versus biologics. Patients generally prefer the oral route, as it has economic savings, better racial equity, and less environmental toxicity versus biologics.

Kristina Callis-Duffin, MD, emphasized the higher comparative efficacy of biologics (achieving PASI90) at the top rankings compared to oral drugs. Moreover, when comparing safety measures, there is no clustering of severe adverse effects to suggest the safety advantages of orals. Dr. Callis-Duffin also mentioned the data from retrospective cohorts in which biologic-exposed patients had a reduced risk of developing psoriatic arthritis (PsA) compared to the control group.\(^5\) On the other side, some studies have shown that systemic (orals and biologics) could reduce the risk of developing PsA.\(^6,7\) Finally, Dr. Callis-Duffin reviewed real-world scenarios of patients with mild-moderate disease for which a biologic can be considered (e.g., nail disease, renal disease, axial PsA).

References
3. Deucravacitinib Versus Placebo and Apremilast in Moderate to Severe Plaque Psoriasis: Efficacy and Safety Results from the 52-week, Randomized, Double-Blinded, Phase 3 Program for Evaluation of TYK2


Late-Breaking Research - Session 1: High Induction Dosing of Risankizumab in Patients with Moderate-to-Severe Plaque Psoriasis: 52-week Results from Phase 2 KNOCKOUT Study

Andrew Blauvelt, MD, MBA, IPC Board Member
Blauvelt Consulting, LLC, Lake Oswego, Oregon, United States

The KNOCKOUT study is a phase II, double-blinded, single-center study using high doses of Risankizumab (300 and 600 mg) to induce long-term remission by decreasing T resident memory cells (Trm) cell number in psoriatic skin. Andrew Blauvelt, MD, MBA, started the presentation by providing the background of the study regarding the well-known crucial role of IL-23 in the pathogenesis of plaque psoriasis, affecting Trm cell retention and proliferation. 1-5

The objectives of this study are to evaluate the number of Trm cells between baseline and week 52 with high doses of Risankizumab, to evaluate the clinical efficacy (skin clearance) with those doses, and to assess its safety. Adult patients with moderate to severe plaque psoriasis was randomized 1:1 to receive either Risankizumab 300 mg or 600 mg subcutaneous at weeks zero, four, and 16, with no further treatment. Trm cells were analyzed by examining lesional and non-lesional skin biopsies at weeks zero and 52. The primary endpoint is to evaluate the change in Trm number from baseline to week 52, while secondary endpoints were PASI100 response at weeks 28, 40, and 52 and safety at week 52. In total, 20 patients were recruited, ten in each arm, and 16 of those patients completed the week 52 visit. At week 52, high induction doses reduced the number of epidermal Trm cells, returning to baseline non-lesional skin levels. High efficacy was shown when PASI75, 90, and 100 responses were measured. Absolute PASI scores at week 52 were below five points in the total population. This dosing regimen was generally well-tolerated, and no new safety signals were observed.

In conclusion, Trm cell count reductions were observed with high induction dosing, which may explain the cellular rationale for the durability of skin clearance noted among patients. Further prospective studies are needed to evaluate the therapeutic potential of these findings of long-term remission.

References
Late-Breaking Research - Session 1: The Light Treatment Effectiveness (LITE) Study: A Pragmatic Trial of Home vs Office Based Narrowband UVB Phototherapy for the Treatment of Psoriasis in the US

Joel Gelfand, MD, MSCE, IPC Board Member
University of Pennsylvania, Philadelphia, Pennsylvania, United States

Phototherapy is still a cost-effective and safe alternative for treating psoriasis patients. Office phototherapy is 10-100 times less expensive than biologics for psoriasis. It has also shown similar efficacy as Adalimumab with better patient-reported outcomes from randomized control trials.1-3

Joel Gelfand, MD, MSCE, introduced the LITE study, a patient-centered study in which the main hypothesis was that home-based narrowband UVB phototherapy treatment would be non-inferior to office-based according to outcomes that matter to patients, providers, and payers. Co-primary outcomes were PGA 0/1 and DLQI ≤ 5. The study population was patients older than 12 with plaque or guttate psoriasis and candidates for phototherapy. They were randomized 1:1 to office or home-based phototherapy for 12 weeks, followed by a 12-week observational period. About 12% of the population used biologics or non-biological systemic therapy at the time of randomization. Home phototherapy demonstrated non-inferior efficacy compared to office-based (PGA 0/1 and DLQI) with statistical significance across all skin types. Cumulative dosing (in Joules) was higher among home-treated patients, with a higher percentage of episodes of “more than 48-hour erythema”. About 60% of the subjects achieved a clear/almost clear response, and nearly 50% achieved a 90% reduction in BSAxPGA.

References

Late-Breaking Research - Session 1: Efficacy and Safety of ESK-001, a Highly Selective Oral TYK2 Inhibitor, in a Phase 2 Study in Adults with Moderate-to-Severe Plaque Psoriasis (STRIDE)
Kim Papp MD, PhD, FRCPC
President and Director of Research, Probity Medical Research Inc., Waterloo, Ontario, Canada

ESK-001 is a highly selective allosteric TYK-2 inhibitor with robust PK/PD correlation (maximal inhibition of type-I IFN gene signature achieved at highest dosing and maintained across 24-hour dosing periods). Kim Papp MD, PhD, FRCPC presented the results of phase two STRIDE study and open-label extension (OLE) studies. Both phase two study and the OLE study included safety and efficacy endpoints. Regarding efficacy endpoints, there was an apparent dose-dependent effect with maximal TYK-2 inhibition achieved at the highest dose (40 mg BID). The STRIDE study demonstrated significant improvement in all PASI and sPGA responses with higher doses. In contrast, the OLE study showed significant efficacy over time at week 16 (PASI75, 90, and 100 were observed in 90%, 57%, and 35% of subjects, respectively. In general, ESK-001 was safe and well-tolerated across dose levels, most treatment-related adverse effects were mild, and long-term exposure to OLE continued to show its favorable risk-benefit profile.
FRONTIER 1 was a phase two, randomized, double-blind, placebo-controlled trial that evaluated the efficacy and safety of JNJ-77242113 (IL-23 receptor inhibitor) in patients with moderate to severe psoriasis. The FRONTIER 2 study corresponds to the long-term extension through one year of observation. Laura Ferris, MD, PhD, presented the results of the FRONTIER 2 study.

The aim was to evaluate the efficacy and safety of the drug administered across a range of doses over one year in patients with moderate to severe psoriasis. Patients continued their dose regimen without any changes from the FRONTIER 1 study, except from the placebo arm that switched to JNJ-77242113 100 mg QD. The results provide data on a sustained response through week 52, with PASI75 response rates from 48.8% to 76.2% among different doses. Patients who crossed over from placebo to the studied drug had a PASI75 response that rapidly converged to those observed with the active drug. Clinical efficacy was also maintained from week 16 through week 52 in the groups that showed PASI90 and PASI100 responses. The highest response rates were achieved in the 100 mg BID group. The most common adverse effects were nasopharyngitis, upper respiratory tract infections, and COVID-19. No evidence of a dose-dependent increase in the occurrence of adverse effects was noted.
Late-Breaking Research - Session 1: Efficacy and Safety of Apremilast for the Treatment of Japanese Patients with Palmoplantar Pustulosis: 16-week Results from a Phase 3, Randomized, Placebo-Controlled Trial

Tadashi Teuri, MD, PhD, IPC Councilor
Nihon University School of Medicine, Tokyo, Japan

Palmoplantar pustulosis (PPP) is a chronic disease with limited treatment options, and its pathogenesis implies Th1, Th2, and Th17-derived inflammatory cytokines. Phosphodiesterase-4 inhibition is known to increase cAMP, which results in an inhibition of these cytokines.\(^1\)\(^-\)\(^7\) Findings from a phase two, placebo-controlled Apremilast study revealed efficacy and safety for its indication in moderate to severe PPP.\(^8\)

Tadashi Teuri, MD, PhD, presented a randomized, placebo-controlled trial performed among Japanese patients with moderate to severe PPP with inadequate responses to topicals. In total, 176 patients were recruited, randomized 1:1 to Apremilast 30 mg BID and placebo, with a cross-over from placebo to Apremilast from week 16 until week 52 in the extension phase. The primary endpoint was PPPASI-50 response at week 16 (≥50% reduction in PPPASI total score). Secondary endpoints were PPPASI total score change from baseline at week 16 and PPSI total score change from baseline at week 16. Subjects were eligible if PPPASI total score was ≥ 12, with pustules/vesicles severity score ≥2 and inadequate response to topicals. Patients with plaque psoriasis and those with pustules beyond the palmoplantar region were excluded. The mean PPPASI total score was 22.1, and tobacco use was observed in 47.2% of patients. PPPASI-50 response at week 16 was significantly higher in the treatment arm (67.8% vs 35.3%, p<0.0001). Secondary endpoints such as PPPASI and PPSI total score change from baseline also showed significant differences. Safety findings were consistent with the known Apremilast-safety profile (diarrhea, soft feces, nausea, headache). In the setting of limited oral treatment options for this condition, Apremilast has shown effectiveness and a good tolerability profile.

References


Late-Breaking Research - Session 1: Bimekizumab Efficacy from Treatment Initiation Through 4 Years in Patients with Plaque Psoriasis: A Comprehensive, Long-Term, Pooled Analysis from BE BRIGHT

Mark Lebwohl, MD, IPC Councilor
Icahn School of Medicine at Mount Sinai, New York, New York, United States

Bimekizumab is a monoclonal antibody that targets both IL-17 A/F and has shown rapid and superior efficacy in treating plaque psoriasis.\(^1\)\(^-\)\(^6\) The objectives of this study were to evaluate the efficacy responses from Bimekizumab initiation through four-year follow-ups, together with reporting clinical and health-related quality-of-life outcomes over those four years.

Mark Lebwohl, MD, PhD presented data from the BE BRIGHT study, which corresponds to an open-label extension from year one up to year four of treatment for those patients that were previously enrolled in the BE-SURE, BE-VIVID, and BE-READY studies. Patients who previously had PASI response <90 were maintained with Bimekizumab 320 mg every four weeks, and those with PASI ≥90 were treated with every eight weeks. Relevant efficacy endpoints considered were: PASI90, PASI100, PASI≤2, BSA≤1%, and DLQI 0/1 through year four. In total, 771 patients entered the open-label extension; 40% of this population experienced biologics, and 83% completed the four-year follow-up. Results showed that PASI90 responses over four years remained stable (88% of patients), with PASI100 responses in 72.6% of the overall population. In summary, Bimekizumab showed high rates of clinical and health-related quality-of-life responses, which were highly durable in the long term through four years of follow-up.

References

Late-Breaking Research - Session 1: Guselkumab Showed Good Efficacy in Treating Generalized Pustular Psoriasis with Low Relapse Rate and Reduction in CD8+ Tissue Resident Memory T Cells
Yuling Shi, MD PhD (on behalf of Jiajing Lu, MD, PhD), IPC Councilor
Department of Dermatology, Shanghai Skin Disease Hospital. School of Medicine, Tongji University, Shanghai, China

The IL-36 pathway has been recognized to play a crucial role in the pathogenesis of generalized pustular psoriasis (GPP). Yuling Shi, MD, PhD, highlighted the severity and potential morbidity of GPP.

Dr. Shi presented a study that included adults with confirmed diagnoses of GPP who did not respond to previous treatments. This study had three groups: Adalimumab, Secukinumab, and Guselkumab, each associated with Acitretin 20 mg/daily. A total of 50 patients were enrolled: 15 were on Adalimumab, 19 on Secukinumab, and 16 on Guselkumab. Efficacy was shown after 12 weeks of treatment, with decreased disease severity (GPPASI, BSA) and quality of life (DLQI). The effects of Secukinumab and Guselkumab were more evident than Adalimumab. Guselkumab had faster elimination of pustules and shorter hospital stays.

Since the COVID-19 pandemic, all groups had to discontinue biologics due to the unknown risks associated with COVID-19 at the time. However, they continued Acitretin. Guselkumab-treated patients also experienced a longer time to relapse. By immunofluorescence staining, skin lesions showed changes in T resident memory (Trm) cells (CD69+, CD103+), with a proportion of Trm CD8+ cells that decreased significantly after Guselkumab treatment.
The Translational Revolution in Inflammatory Skin Diseases
Mark Lebwohl, MD, IPC Councilor
Icahn School of Medicine at Mount Sinai, New York, New York, United States

Over the last decades, there have been advances in our knowledge of psoriasis pathogenesis. It is well-known that we have switched from a keratinocyte-based to an immunology-based model.\(^1\) Due to these findings, multiple drugs have been and continue to be developed. Multiple specific inflammatory targets have been used for therapeutic drug inhibition.

With psoriasis, IL-23 blockage determines the inhibition of Th17 cells and the consequent reduction of IL17, a cytokine that plays a key role in psoriasis.\(^1\) If IL-23 is blocked, the Th17 stops working, and the inflammation significantly reduces. This class of biologics has demonstrated excellent responses.

In the field of atopic dermatitis, evidence shows the relevance of Th2-driven inflammation, with IL-4, IL13, and IL-31 as critical mediators.\(^2\) Drugs targeting these pathways have also demonstrated excellent clinical efficacy in this population. (Dupilumab: IL-4, IL-13; Tralokinumab/Lebrikizumab: IL-13; Nemolizumab: IL-31).

Knowledge about generalized pustular psoriasis (GPP) has expanded as IL-36 is recognized as a critical player in its pathogenesis. The efficacy of IL-36 receptor inhibition (Spesolimab) has been shown in EFFISAYIL 1-2 studies, with rapid pustular clearance as fast as week one.\(^3\) Other uses of this drug have been studied, for example, in recalcitrant pyoderma gangrenosum.

Finally, we have the new trending family of drugs: JAK inhibitors.\(^4,5\) From drugs that generate a pan-JAK non-selective inhibition, new developments have been made towards a more specific JAK blockage. We have TYK2 inhibitors, such as Deucravactinib, which block part of the signaling of IL-23 receptors.

References
Psoriasis: A Model Disease for Therapeutic Targeting  
Bruce Strober, MD, PhD, IPC Board Member  
Central Connecticut Dermatology, Cromwell, Connecticut, United States

The importance of the new developments during the last decades has led to optimism towards the future in the field.\(^1\)\(^2\) Some of the first drugs for managing psoriasis are acitretin, cyclosporine, and methotrexate.\(^3\) Over time, there was a shift from a keratinocyte-based physiopathology in psoriasis to an inflammatory/T cell-mediated (cytokine signaling). This modulation by cytokine signaling in psoriasis was recognized primarily by the observation of good clinical effects of drugs such as cyclosporine. Dr. Strober mentioned the role of danger-recognition cells (NK cells, plasmacytoid dendritic cells, macrophages) in initiating the inflammatory cascade by releasing IFN-gamma and TNF-alpha. He highlighted the role of TNF-alpha inhibitors in the setting of targeted biologics.

A new paradigm was reached between 2006 and 2010 with Adalimumab and Ustekinumab (both with 70% overall response). As new drugs have emerged, there is less frequent dosing and better responses. Inhibition of the IL17 pathway has shown the pivotal role of this target in psoriasis. Between the years 2014 and 2017, new highly effective drugs were available: Apremilast (30% response), Secukinumab (80% response), Ixekizumab (90% response), and Brodalumab (85% response.) From 2017 to 2019, IL23 inhibitors and Certolizumab pegol development came through, together with Risankizumab, Tildrakizumab, and Guselkumab.

Where are we now? Dr. Strober emphasized the ongoing oral medication studies. The FRONTIER 1-2 studies have proven the effectiveness of a first-in-class oral peptide that blocks the IL-23 receptor and potently antagonizes the IL-23 signaling.\(^5\) Efficacy data showed that 78.6% of patients reached a PASI 75 response at 16, 59.5% with a PASI 90 response, and 40.5% with a PASI 100 response.

Another new oral development is TYK-2 inhibition with Deucravactinib (SOTYKTU), which is already on the market. New molecules (TAK-279) are also in development, which have a greater affinity for TYK-2 and may improve response rates.

In conclusion, diverse scientific advances have expanded psoriasis treatment, with notable contributions from biologics and new oral targeted and topical medications.

References

Update on Pipeline Therapies for Psoriasis
Bruce Strober, MD, PhD, IPC Board Member
Central Connecticut Dermatology, Cromwell, Connecticut, United States

Bruce Strober, MD, PhD, started his presentation by recognizing the importance of maximizing the inhibition of all IL-17 signaling. He introduced the recently US-approved drug (Bimekizumab), which has dual inhibition of IL17A/F and neutralizes the isoforms IL17 A/A, A/F, and F/F. According to the BE READY study, more than 90% of patients reached PASI 90 response at week 16, with persistence of response until 52 weeks. The drug safety profile also did not raise any major concerns, presenting mucosal candidiasis due to IL17-F inhibition between 10-15% of patients. Pooled data from five phase three randomized control trials with Bimekizumab have also shown high efficacy in nails and scalp psoriasis and good retention of efficacy after a two-year follow-up.

Dr. Strober then discussed a head-to-head comparison between Risankizumab and Apremilast. A phase four, randomized, open-label, assessor-blinded study compared both drugs among patients with moderate and severe psoriasis. Initial randomization was made to Risankizumab 150 mg subcutaneously or Apremilast 30 mg BID. After 16 weeks, Apremilast patients were re-randomized 1:1 to either continue Apremilast or Risankizumab. The efficacy of Risankizumab was significantly higher than that of the Apremilast group (56% vs. 5% patients achieving PASI90; 75% vs. 18% patients achieving PGA 0/1). Risankizumab was better tolerated than Apremilast but showed slightly more COVID-19 cases.

So, do patients prefer oral or subcutaneous treatment? The answer, however, is not simple, as several factors must be considered in the decision, such as tolerability, cost, access, laboratory monitoring, and comorbidities.

Dr. Strober then began discussing pipeline therapies:

IL-36 Receptor Antibody
In the generalized pustular psoriasis (GPP) field, the EFFISAYIL-1 study demonstrated the efficacy of Spesolimab (anti-IL-36 receptor antibody) for treating flares. The primary endpoint was the percentage of patients with GPPPGA pustulation subscore of 0 (no visible pustules) at week one, which was achieved in 54% of subjects treated with Spesolimab 900 mg IV versus 6% in the control group. The EFFISAYIL-2 study was a phase two randomized, dose-ranging trial of Spesolimab for flare prevention. Subjects were randomized into four arms: high/medium/low-dose regimens and placebo. The primary endpoint was time to GPP flare by week 48. The high-dose regimen yielded an 84% reduction in risk for flare development.

TAK-279: New Molecule as Oral TYK-2 Inhibitor
Since the approval of Deucravactinib, new drug development has been underway to maximize TYK2 specificity. There has been a phase 2b study with promising results as it demonstrated higher efficacy than reported in Deucravacitinib studies. Acne and acneiform dermatitis were the most relevant detected adverse effects.
Oral IL-23 Receptor Antagonist (JNJ-77242113)
FRONTIER-1 was a dose-ranging trial that evaluated the efficacy and safety of this molecule at 16 weeks among patients with moderate to severe psoriasis. Subjects were randomized to five different dosing arms of the drug or placebo during a 16-week follow-up time and afterward could either continue to an LTE (FRONTIER-2) or a final four-week follow-up. The primary endpoint was a percentage of patients achieving PASI75 at week 16, which reached 78.6% of subjects with higher dosage versus 9.3% in the placebo group. There were no relevant safety issues.

VISIBLE Cohort
This study observed the efficacy of Guselkumab for skin color patients with a unique evaluation of the consequences for the patients due to discoloration caused by psoriasis. Patients were randomized to Guselkumab versus placebo for 16 week-period, and beyond that time, patients received Guselkumab 100 mg. The Skin Discoloration Impact Evaluation Questionnaire (SDIEQ) was significantly improved at 16 weeks using Guselkumab vs placebo and ss-IGA 0/1 and PSSI90.

References
Early Treatment of Psoriasis: A Window of Opportunity?
Richard Langley, FRCP, FACP, IPC Councilor
Dalhousie University, Halifax, Canada

Data from pivotal randomized clinical trials evaluating disease duration among populations show that of patients between 15 and 20 years old, 25-50% of them have not received a biologic.\textsuperscript{1} Richard Langley, MD emphasized the importance of the “cumulative life course impairment,” which could be minimized with early treatment. If the conception of psoriasis broadened as an inflammatory, multisystem disorder, then inflammation in the skin could potentially affect other domains.

Dr. Langley suggests that the window of opportunity to treat patients correlates with an earlier diagnosis and the possibility of altering the long-term trajectory of the disease.\textsuperscript{2} A study performed by Kimball et al. showed that about 20% of psoriasis patients had undiagnosed diabetes, hypertension, or hypercholesterolemia.\textsuperscript{3} In addition, 40%-60% did not have those conditions optimally managed.

Based on the PSOLAR cohort, which evaluated the impact of systemic treatment on mortality risk (Methotrexate, Ustekinumab, and TNF-alpha inhibitors), it showed that short- and long-term treatment with biologics was associated with lower risks of all-cause and cardiovascular mortality versus no exposure.\textsuperscript{4}

Dr. Langley then questioned if biologic treatment reduces the risk of developing psoriatic arthritis (PsA).\textsuperscript{5-7} The PAMPA trial is a multicenter study in which subjects are initially randomized to either Guselkumab or placebo.\textsuperscript{8} The co-primary endpoints are changes from baseline MSK-PDUS (musculoskeletal power Doppler US) and the percentage of patients transitioning to PsA. This trial will bring new valuable data to help answer the articular disease prevention dilemma.

The concept of “molecular scar” in psoriasis was also discussed, representing the persistence of T resident memory (Trm) cells in previously affected skin areas with psoriasis. The GUIDE part three study considered early disease patients and their potential to maintain response for long-term treatment-free periods.\textsuperscript{9} Patients with disease duration <15 months remained treatment-free significantly longer than those with a more prolonged disease course. This observation may be explained by the concept of “molecular scar.”

As a final comment, Dr. Langley shared that early treatment may result in higher response rates and chances for remission. There has also been preliminary but promising data on preventing disease comorbidity and progression.

References


Impact on Comorbidities for Biologic Selection for Psoriasis

Jeffrey Marcus Cohen, MD
Yale School of Medicine, Branford, Connecticut, United States

Biologics have revolutionized the treatment of psoriasis. Medications with high effectiveness are generally safe but with some considerations that prompt personalized care. Psoriasis is known to be associated with different comorbidities, so it is essential to consider when selecting treatment. For example, psoriatic arthritis (PsA) tends to develop 10-12 years after psoriasis diagnosis.

Inflammatory bowel disease (IBD) has also been associated with psoriasis, and the risk is increased with concomitant PsA. According to case-control studies, Crohn's disease and ulcerative colitis have demonstrated higher incidence among psoriasis patients (OR 1.7 and 1.75, respectively). Interleukin-17 inhibitors are contraindicated for psoriasis patients with IBD as different trials have shown data of increased number or worsening of IBD.

Hepatitis B infection and other infections also need to be encompassed due to potential reactivation in HBsAg-positive cases. Hepatitis B virus reactivation has been less common with antiviral prophylaxis. Hepatitis C reactivation entails minimal risk, with increases in viral loads but uncommon viral reactivation. Newer generation biologics (IL17, IL23 inhibitors) have limited data in this area but appear safe. Hepatology consultation is recommended for a multidisciplinary approach to these patients. The human immunodeficiency virus represents a challenge while treating psoriasis patients. The safest use of biologics or another immunosuppressive drug should consider suppressed viral loads, normal CD4 counts, and patients taking antiretroviral therapy.

Another well-known psoriatic comorbidity is congestive heart failure (CHF). Jeffery Marcus Cohen, MD emphasized the concept that TNF-alpha inhibitors may increase mortality in patients with chronic heart failure due to decompensation or even new onset of CHF. Demyelinating disease such as multiple sclerosis may also be associated with psoriasis, and patients treated with TNF-alpha inhibition have shown more exacerbations of their neurologic disease.

Finally, Dr. Cohen remarked on the increased risk of malignancy among the psoriasis population, especially keratinocyte-derived carcinomas and lymphoma. Currently, biologic use in psoriasis patients with malignancy has limited data based on case series or retrospective studies.

References


Clinical Considerations in Managing Women with Psoriasis
Jennifer Soung, MD
Southern California Dermatology, Santa Ana, California, United States

It is crucial to have a gender-sensitive approach to psoriasis.¹ Women tend to report higher DLQI scores than men despite showing lower PASI scores, and women also experience higher stigmatization because of the disease.² One clinical subtype of psoriasis that is particularly frequent among females is palmoplantar pustulosis. If we analyze female psoriatic arthritis (PsA) patients, polyarthritis tends to be the most common presentation.

Jennifer Soung, MD, also pointed out the relationship between hormones and psoriasis. During menopause, almost half of women had an exacerbation of psoriasis, and late-onset psoriasis is more common in women than men. In a Korean cohort, it showed that the most prolonged duration of hormone replacement therapy was significantly associated with a higher risk of developing psoriasis.³ On the other hand, pregnancy status tends to improve psoriasis, which is speculated to come from very high levels of estrogen and immune shift towards Th2 inflammation.⁴

The genetic basis of psoriasis also implies the importance of family planning and our role in genetic counseling. There is frequent fear from mothers to transfer their disease to their children. Dr. Soung presented the results from a systematic review that included more than 4,500 pregnancies. The conclusion was that there are no increased or poor outcomes in pregnant women or their fetuses. In Dr. Soung’s practice, mothers are treated case by case. Generally, she recommends stopping psoriasis treatment unless the mother has a prior history of active psoriasis, arthritis during pregnancy, or a history of pustular psoriasis during pregnancy. Certolizumab pegol is one of the safest options for mothers due to its null or minimal placental and milk transfer.⁵ IL17 or IL23i have shown an average duration of action for about six months so that clearance could be maintained after discontinuation during the first trimester. Post-partum is a generally critical period for mothers because of potential flares, less-treated patients, and the Koebner phenomenon on the nipples.

References
Comparative Efficacy and Relative Ranking of Psoriasis Biologics with Real-World and Clinical Trial Data
Mona Shahriari, MD
Yale University School of Medicine, New Haven, Connecticut, United States

Dr. Mona started her presentation by explaining that comparisons between biologics should be made based on data derived from head-to-head clinical trials, network metanalyses, and real-world evidence. Mona Shahriari, MD, presented several head-to-head clinical trials.

The first head-to-head comparison presented was the UNCOVER study in which both doses of Ixekizumab (80 mg q4 weeks and 80 mg q8 weeks) showed superiority to Etanercept. The SPIRIT trial was a head-to-head comparison of Ixekizumab versus Adalimumab, where Ixekizumab was superior to Adalimumab in the proportion of patients achieving both PASI100 and ACR50 at week 24. Ixekizumab was comparable to Adalimumab in the ACR50 responses at week 24. The ECLIPSE trial compared Guselkumab versus Secukinumab, showing that Guselkumab was superior to Secukinumab in the proportion of patients achieving PASI90 at week 48 and was non-inferior in PASI75 responses at week 12 (rapid response). The IMMerge study compared Risankizumab versus Secukinumab showing higher efficacy for the IL23i (in the proportion of PASI90 at week 52) and non-inferiority to Secukinumab in the proportion of patients achieving PASI90 at week 16. The IXORA-R trial used Ixekizumab versus Guselkumab and demonstrated that Ixekizumab was superior to Guselkumab in the proportion of patients achieving PASI100 at week 12 and was non-inferior to Guselkumab at week 12. The BE VIVID trial compared Bimekizumab versus Ustekinumab and showed that significantly more patients receiving Bimekizumab achieved PASI90 and PGA 0/1 at week 16, with also faster onset. Bimekizumab has also been compared head-to-head with Secukinumab (BE RADIANT), showing superiority at PASI100 at week 16.

Dr. Shahriari also highlighted the advantages of network metanalyses due to direct and indirect comparisons between all available drugs for psoriasis, allowing a treatment ranking. According to a network meta-analysis by Armstrong et al., Bimekizumab showed the best short-term efficacy (10-16 weeks); meanwhile, Risankizumab had the highest benefit safety in the long-term profile.

Real-world data from the PSOLAR study, which involved over 2,000 patients, was presented. It showed that the overall effectiveness of Ustekinumab was significantly better than that of TNF-alpha inhibitors. Finally, Dr. Shahriati showed results from the CorEvitas cohort, in which Guselkumab had significantly higher drug persistence than Secukinumab and Adalimumab in bio-naive and bio-experienced patients.

References


Translating AAD/NPF Guidelines to Your Clinical Practice to Lower Cardiovascular Risk in Patients with Psoriasis

Joel Gelfand, MD, MSCE, IPC Board Member
University of Pennsylvania, Philadelphia, Pennsylvania, United States

There is a high number of publications dealing with psoriasis and cardiovascular disease (CVD). Several pathophysiological factors mediate the inflammatory milieu and promote cardiovascular risk, such as Th1/Th17 (related to atherosclerosis, thrombosis, lipid metabolism), epidermal proliferation (linked to higher uric acid and oxidative stress, and angiogenesis (linked to endothelial dysfunction). The higher CV risk of these patients has vital importance as previously demonstrated an increased risk of myocardial infarction, stroke, cardiovascular death, diabetes, and chronic kidney disease.

Joel Gelfand, MD MSCE, presented a recent study that showed that increases in PASI scores were an independent risk factor for CV events. Meta-analysis studies have also demonstrated augmented risk of cardiovascular outcomes being higher among severe patients compared to mild psoriasis. One key point that Dr. Gelfand highlighted was that the risk of CVD associated with autoimmunity increases with age.

Dr. Gelfand presented a systematic review and meta-analysis that showed that the most substantial reduction in blood-based cardiometabolic risk biomarkers was seen with Adalimumab and phototherapy. By contrast, a publication from a nationwide French study of psoriatic arthritis (PsA) patients associated IL12/23 and IL17 inhibitors with increased risk of MACE versus TNF-alpha inhibitors. Comprehensive, evidence-based studies have not yet demonstrated the overall benefit of any biologic, oral JAKi, or PD4 antagonist.

Immune-targeted drugs may have paradoxical events with worsening instead of improvement. Some data suggest that TNF-alpha inhibitors are likely the most cardioprotective of current psoriasis treatments, but data are inconclusive. To date, only Colchicine and Canakinumab have been demonstrated to be effective in lowering cardiovascular risks.

References


Treating Psoriasis while Preventing Psoriatic Arthritis: What are the Early Data?
Kenneth Gordan, MD, IPC Councilor
Medical College of Wisconsin, Milwaukee, Wisconsin, United States

Kenneth Gordon, MD, showed the model of progression from psoriasis to the development of preclinical, subclinical, and prodromal psoriatic arthritis. Dr. Gordon emphasized the importance of early diagnosis, with a “window of opportunity” from the initial stages before the symptoms appear.

Data from the Optum Clinformatics (2007-2011), a retrospective cohort study, evaluated the development of psoriatic arthritis (PsA) among patients with biologics for psoriasis. There were two cohorts: one on phototherapy treatment and the other one with biologics. Biologic use was associated with a significantly lower risk of PsA development compared to phototherapy users.

Dr. Gordon also mentioned the TriNetX network that evaluated the time of incident inflammatory arthritis among biologic users from a US sample using electronic health records. The results showed that lowering the risk of incident inflammatory arthritis was significant in the sensitivity analysis from IL-12/23 and IL-23 users compared to TNF-alpha inhibitors. The IL-17i showed a risk reduction, but it was not significant.

Data from the Optum database analysis demonstrated that patients receiving IL-23i had numerically lower incidence rates of inflammatory arthritis than other biologics. While the observational studies are needed and informative, Dr. Gordon shared the limitations of current observational approaches dealing with incomplete measurement of potential confounding variables, selection bias, collider bias, and observation bias, among others.

As such, the PAMPA trial, a multicenter study in which patients were randomized to Guselkumab or placebo, has acknowledged the need for randomized controlled trials to answer this question better. After 24 weeks, both arms were also compared to an observation group without the study drug. No data is available for this trial; however, Dr. Gordon expects this trial can help provide data in this field and start to fill the gap.

Dr. Gordon closed the presentation by sharing that large claims database approaches tend to suggest that blockades of IL-23 can impact articular disease prevention, but these findings are inconclusive.

References
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New and Emerging Biologics
Kenneth Gordon, MD, IPC Councilor
Medical College of Wisconsin, Milwaukee, Wisconsin, United States

Numerous treatments are currently available for psoriasis patients. Kenneth Gordon, MD, discussed newer treatment strategies, such as smaller peptides (nanobodies) that can be given orally. He asked the audience, “Why are there so many biologics for psoriasis?” He answered that psoriasis has a very straightforward immunological pathway and that it is easier to measure cutaneous disease activity in a clinical trial.

Dr. Gordon then discussed new drugs, including Bimekizumab, JNJ-2113, and Sonelokinab. Bimekizumab is the latest approval in the United States, while it has been available for some time in other countries. Bimekizumab has high efficacy with maintenance of response after three years of follow-up in psoriasis and even higher compared to other biologics in psoriatic arthritis (PsA).¹⁻³

The development of JNJ-2113, the oral nano peptide that blocks the IL-23 receptor, could be very promising if IL-23 is considered one of the most important cytokines in the psoriasis inflammatory cascade. Another new drug option, Sonelokinab (M1095), an IL-17 A/F directed nanobody, has three times more IL-17 binding sites per mg versus conventional antibodies.⁴

He concluded with excitement about biologic therapy for psoriasis and the continued development of new therapies.

References
Psoriasis Comorbidities
Julia-Tatjana Maul, MD, IPC Councilor
University Hospital Zurich, Zurich, Switzerland

Julia-Tatjana Maul, MD, introduced the concept of psoriasis as a chronic systemic inflammatory skin disease, making it a complex and heterogeneous disease. Chronic inflammation is a basal state that determines the initiation of comorbidities. As the disease develops over time, a cumulative life course impairment is observed in patients. All doctors, especially dermatologists, have the challenge and responsibility to initiate treatment early to minimize future morbimortality.

Dr. Maul showed the frequency of comorbidities in psoriasis grouped into four main categories: metabolic, psychiatric, cardiovascular, and autoimmune/immune-mediated. Comorbidity is common, may reduce response to therapy, and can increase morbidity and mortality. Patients may have multiple comorbidities at once, and this determines the decisions and the prognosis.

Concerning psoriatic arthritis, 20% of patients have progressive joint destruction like rheumatoid arthritis. Dr. Maul also highlighted obesity as a risk factor for treatment failure, as data has shown increases in the rates of inadequate responses associated with higher BMI scores. Obesity is a risk factor for other diseases as well, including atherosclerosis, insulin resistance, and depression.

Cardiovascular risk and metabolic syndrome are other main concerns as comorbidities among patients that require multidisciplinary care. Psychiatric problems, especially mood disturbances and anxiety, are also more common in pediatric and adult populations with psoriasis.

In final remarks, Dr. Maul emphasized that comorbidity is an essential factor in psoriasis, which can be manageable and requires patient self-responsibility and empowerment.

References