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A Report from the 2024 Society for Investigative Dermatology Annual Meeting (SID)

Evan Austin, MD, PhD

SUMMARIZING SESSIONS WITH A FOCUS ON PSORIASIS

INTRODUCTION

The Society for Investigative Dermatology (SID) held its 2024 Annual Meeting in Dallas, Texas, from May 14-18, 2024. The five-day event included the International Psoriasis (IPC) Council Symposium: Advances in Technologies and Analytics in Understanding Psoriasis Pathophysiology. This congress report includes a summary of the IPC symposium presentations and nine other crucial psoriasis sessions throughout the congress.

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The Microbiome and Psoriasis

Wilson Liao, MD, IPC Councilor

University of California, San Francisco, San Francisco, California, United States

Wilson Liao, MD, IPC Councilor, provided an insightful overview of the microbiome's role in psoriasis. The microbiome plays essential roles in developing and activating the immune system, protecting against pathogens, aiding digestion, and producing essential vitamins.

Dr. Liao focused on four key areas regarding the microbiome and psoriasis: its role in triggering psoriasis, its relation to comorbidities like psoriatic arthritis, its influence on medication responses, and the potential for therapeutic manipulation.

Several studies have examined the skin microbiome in psoriasis, highlighting a consistent dysbiosis compared to healthy controls.¹ Notably, beneficial bacteria like *Cutibacterium acnes* are decreased,² while harmful bacteria like *Staphylococcus aureus* are increased in psoriatic skin.³ Experiments indicated that *Staphylococcus aureus* might activate psoriasis-related immune pathways.

The gut microbiome in psoriasis also shows significant differences, with increased *Firmicutes* and decreased *Bacteroidetes* associated with conditions like obesity, type 2 diabetes, and cardiovascular diseases. Specific bacteria, such as *Faecalibacterium prausnitzii* and *Eubacterium rectale*, which produce anti-inflammatory short-chain fatty acids, are also decreased in psoriasis patients.

Dr. Liao shared that the gut microbiome may influence psoriasis severity and comorbidities, including psoriatic arthritis. In addition, gut dysbiosis in psoriatic arthritis patients resembles that in inflammatory bowel disease, indicating a potential link. Lastly, Dr. Liao discussed how the gut microbiome might predict responses to treatments like methotrexate and that diet and probiotics can alter the gut microbiome and impact psoriasis/

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TCR Analysis Using Genomics Data

Emanuel Maverakis, MD

University of California Davis, Sacramento, California, United States

Emanuel Maverakis, MD, delivered a talk focusing on T-cell receptor analysis and its implications for psoriasis. He outlined the foundational concepts of T-cell receptor diversity, highlighting that gene rearrangement processes enable the creation of a vast array of T-cell receptors. Although the human body utilizes only some of these receptors, this raises questions about the necessity of such diversity.

Dr. Maverakis detailed his research on T-cell receptor segments, specifically TRAJ23 and TRAJ39, which showed distinct expression patterns in psoriasis. Initial bulk RNA sequencing indicated that TRAJ23 was upregulated while TRAJ39 was downregulated in psoriatic skin. Further single-cell sequencing confirmed the presence of TRAJ23 in psoriasis lesional skin, but contrary to expectations, TRAJ39 was also found, though not significantly associated with known psoriasis-related genetic markers.

Dr. Maverakis's team discovered that keratinocytes, the predominant cell type in the epidermis, expressed TRAJ23 but not TRAJ39, suggesting that keratinocyte proliferation in psoriasis could explain the upregulation of TRAJ23. Moreover, fibroblasts were found to express TRAJ39, shedding light on the complex cellular interactions in psoriasis. The expanded T-cell clones in psoriatic skin were predominantly memory T cells, indicating past activation but not current proliferation, as shown by the lack of Ki-67 expression, a cell proliferation marker.

Dr. Maverakis concluded by emphasizing the need for further research to understand the functional roles of these T-cell receptor segments in different cell types and their contributions to psoriasis pathogenesis.

Statistical Genomics and Multi-omic Approaches in Advancing Genetic Research for Psoriasis

Alex Tsoi, MD, PhD, IPC Councilor

University of Michigan, Ann Arbor, Michigan, United States

Alex Tsoi, MD, PhD, presented on applying genome-wide association studies (GWAS) to identify genetic variants linked to complex traits, particularly psoriasis. His recent work analyzed data from over 36,000 psoriasis cases, offering a comprehensive genetic landscape of the disease.¹ He highlighted the importance of understanding disease pathology through case-control comparisons and identifying biomarkers and therapeutic targets. Additionally, he discussed the significance of exploring the heterogeneity among cases to advance personalized medicine.

Dr. Tsoi shared that a key challenge in genetic studies is that many disease variants are non-coding, necessitating the integration of genetic data with other data types to identify involved cell types, gene targets, and mechanisms. He also discussed using multi-omics information to enhance the interpretation of genetic data. His current research utilizes statistical genomics techniques to interpret GWAS results, focusing on the regulatory roles of psoriasis-associated loci in keratinocytes and identifying cell-type origins of cytokines affecting these genetic targets.

Dr. Tsoi uses single-cell data and spatial omics to map gene expression profiles and understand cell-type interactions in psoriasis. He presented data showing how keratinocyte gene expression is influenced by proximity to other immune cells, particularly those producing cytokines like interleukin (IL)-17 and tumor necrosis factor (TNF). His research integrates these findings with pharmacogenomic studies to explore drug response variability in psoriasis, linking genetic variants with treatment outcomes and identifying potential therapeutic targets. This approach aims to bridge the gap between genetic data and clinical applications, enhancing our understanding of psoriasis and improving personalized treatment strategies.

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Towards Personalized Diagnosis and Therapy

Curdin Conrad, MD, IPC Councilor

University Hospital of Lausanne, Lausanne, Switzerland

Curdin Conrad, MD, IPC Councilor, discussed integrating omics data, microbiome studies, and T-cell data into clinical diagnostics and therapy. He emphasized the importance of individualized treatment plans for chronic diseases like psoriasis, where the best treatment option balances efficacy and minimal side effects tailored to each patient's specific conditions and needs.

Dr. Conrad highlighted the progress made in targeted therapies over the past decades, particularly the role of tumor necrosis factor (TNF), interleukin (IL)-23, and IL-17 pathways in psoriasis. He explained that the current approach involves stratifying patients to select optimal therapies based on drug-related factors, patient characteristics, and disease-related factors. He noted that while this method is effective, it is not fully personalized.

He introduced a method involving molecular profiling to create distinct immune signatures for various inflammatory skin diseases, enabling more precise diagnostics and personalized treatment choices. This approach was illustrated through case studies, where patients with ambiguous clinical presentations were successfully treated based on their molecular profiles rather than traditional diagnostics.

Dr. Conrad concluded by discussing the potential applications of this personalized approach in treating different forms of psoriasis, including unstable and pustular psoriasis, emphasizing the need for therapies that target multiple pathways simultaneously. His work underscores the shift towards personalized medicine in dermatology, promising improved patient outcomes through tailored therapeutic strategies.

Granzyme K Promotes IL-23 Secretion and Keratinocyte Proliferation in Psoriasis

Katlyn Richardson

University of British Columbia, Vancouver, British Columbia, Canada

Katlyn Richardson presented on the role of Granzyme K (GzmK) in promoting IL-23 secretion, keratinocyte proliferation, and psoriasis development. GzmK, a serine protease found in the cytotoxic granules of cytotoxic lymphocytes and natural killer cells, was traditionally associated with cell-mediated killing. Recent studies, however, show that GzmK can also accumulate extracellularly, influencing various functions through the cleavage of extracellular substrates, particularly activating protease-activated receptor 1 (PAR-1). This activation leads to the release of pro-inflammatory cytokines and cell proliferation.

The study hypothesized that GzmK mediates keratinocyte proliferation and inflammation in psoriasis via PAR-1-dependent mechanisms. Using a mouse model of psoriasis, it was observed that GzmK knockout mice showed significantly less susceptibility to psoriasis-like symptoms compared to wild-type mice. This was evident from reduced disease severity, epidermal thickness, hyperplasia, immune cell influx, and pro-inflammatory cytokine levels, particularly IL-23.

Further experiments with human keratinocytes confirmed that GzmK induces cell proliferation through PAR-1. Additionally, GzmK stimulation led to phosphorylation of MAP kinase P44/42 and STAT-3, critical pathways in keratinocyte proliferation and psoriasis. This phosphorylation was dependent on PAR-1 activation.

GzmK was shown to induce IL-23 secretion in macrophages, suggesting a mechanism of action similar to that of keratinocytes. These findings highlight GzmK as a promising therapeutic target for psoriasis, offering new avenues for drug discovery and understanding disease mechanisms.

Prevalence and Association of Psoriasis in Patients with Seborrheic Dermatitis: A Systematic Review and Meta-Analysis

Christy Chang

University of Illinois at Chicago, Chicago, Illinois, United States

Christy Chang started the presentation by providing a background on Seborrheic dermatitis (SD) and later discussed the prevalence and association of SD with psoriasis. SD is a common chronic inflammatory skin condition characterized by yellow, greasy scales affecting areas like the scalp, head, neck, and body folds. The clinical manifestations of SD and psoriasis often overlap, leading to frequent co-existence.

Christy Chang and her team conducted a systematic review and meta-analysis, searching various electronic databases for studies with at least 20 healthcare-diagnosed SD participants. They excluded studies focusing solely on one body site or certain populations. Despite screening over 2100 records, only three studies met the inclusion criteria. These included two adult studies and one infant study.

The meta-analysis revealed a prevalence of 2.7% for co-occurring SD and psoriasis, though this estimate showed high heterogeneity, mainly due to the inclusion of infant data. Using a method optimizing for high inter-study heterogeneity, the prevalence for adults was adjusted to 2.1%. The pooled odds ratio was 1.37, indicating no significant association between the conditions. Limitations included the small number of studies and the exclusion of populations with higher SD rates, potentially leading to an underestimation of prevalence.

Christy Chang concluded that the frequency of co-occurring SD and psoriasis in adults is low at 2.1%, with no clear association. More prospective studies are needed to clarify the relationship between SD and psoriasis and to improve specificity in clinical terminology and understanding.

Comparing Itch in Psoriasis, Atopic Dermatitis, and Chronic Idiopathic Urticaria: A Meta-Analysis

Julia L. Gao, MD

Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States

Judy Gao, MD, presented a meta-analysis comparing itch in psoriasis, atopic dermatitis (AD), and chronic idiopathic urticaria (CIU). Historically, psoriasis was considered less itchy than AD or CIU, but recent studies indicate itch might be a significant symptom in psoriasis, warranting its use as a clinical trial outcome.¹⁻⁴

The meta-analysis aimed to compare itch and disease response rates in adults from phase two and three randomized clinical trials involving systemic treatments for these conditions. The systematic search identified 52 trials: 33 for AD, 14 for psoriasis, and five for CIU. The analysis adjusted baseline itch scores to a 100-point scale and calculated pooled non-weighted log odds ratios for disease and itch responses.

Dr. Gao's findings showed AD had the highest mean baseline itch score (71.3), significantly higher than psoriasis (62.6) and CIU (64.4). Disease response in AD was positively correlated with itch improvement. Psoriasis treatments also significantly improved itch scores, with systemic treatments increasing these odds.

Limitations included variability in itch reporting methods across diseases, and AD trials often required a minimum itch score for inclusion, potentially inflating baseline itch scores. Future studies aim to standardize baseline itch scores by BSA involvement.

Key conclusions presented included that psoriasis patients had baseline itch scores similar to CIU patients, and Itch response correlated well with disease response, especially in AD. Dr. Gao believes the study suggests that standardized itch reporting across inflammatory dermatologic conditions would be beneficial. Itch could potentially be an early indicator of disease flares, suggesting treatment should begin at the first sign of itch rather than rash.

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Periodontitis as a Risk Factor for Psoriasis

Rudolf E. Schopf, MD

Johannes Gutenberg University, Mainz, Germany

Rudolf Schopf, MD, presented a study examining the link between periodontal disease (gum disease) and psoriasis, emphasizing the importance of inflammation, bacterial load, and oral hygiene.

In this study, patients provided medical history, including diabetes, hematological disease, HIV infection, smoking habits, family dental history, and periodontal status. Key metrics included the DMFT index (Decayed, Missing, Filled Teeth), bleeding on probing, and depth of gingival pockets.

Results from the study showed that psoriasis patients were more likely to be heavy smokers (more than 20 cigarettes a day), which correlated with poorer periodontal health. Compared to healthy controls, psoriasis patients were less likely to engage in regular tooth brushing, dental visits, and interdental cleaning. Indicators of periodontal disease, such as bleeding on probing and deep gingival pockets, were more prevalent in psoriasis patients. The bacterial load, including specific species like *Tannerella forsythia*, was significantly higher in psoriasis patients. The presence of bacteria associated with the "red complex" was also more prominent. Although not statistically significant, there was a trend toward a more severe inflammatory response in psoriasis patients with higher interleukin (IL)-1 production and reduced receptor antagonist content.

Dr. Schopf shared that psoriasis patients exhibit a higher risk for periodontitis, suggesting that periodontal disease should be considered a comorbidity similar to inflammatory bowel disease, depression, or cardiovascular disease. Maintaining dental health and addressing periodontal disease could potentially reduce psoriasis patients' inflammatory burden.

Heterogeneity of Psoriatic Skin Lesions Identified by a Novel Transcriptomic Based Psoriasis Cell and Immune Score

Peter Lipsky, MD (on behalf of Sneha Shrotri)
Ampel Biosolutions, Charlottesville, Virginia, United States

Peter Lipsky, MD, delivered the presentation on behalf of Sneha Shrotri, which explored the heterogeneity of plaque psoriasis by employing transcriptomic analysis of skin biopsy material.

The study created 48 annotated gene modules representing specific cells and inflammatory processes. Using Gene Set Variation Analysis (GSVA), the expression of these gene modules in skin biopsies from 174 patients with plaque psoriasis was examined.¹

The heat maps generated from this data revealed four distinct patient subsets, each showing different inflammatory and metabolic abnormalities levels. Notably, all patients had increased keratinocyte and neutrophil signatures, confirming their psoriatic condition. However, the groups had significant heterogeneity in other inflammatory and metabolic signatures.

The complex data was then simplified into a Psoriasis Cell and Immune Score (PsoriaCIS), a score designed to evaluate the level of abnormality in each sample. This score differentiated between lesional and non-lesional skin and showed significant differences in molecular severity among the patient subsets despite similar clinical scores. The PsoriaCIS score proved effective in capturing changes in molecular severity with different treatments, reinforcing the score's potential in personalized treatment strategies.

Lastly, Dr. Lipsky shared that the PsoriaCIS score provides a method to grade the molecular severity of psoriatic skin and monitor changes with therapy, supporting personalized treatment approaches in the future.

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Dual Role of Dermal Adipogenesis in Regulating Neutrophil Activation and Regression

Ling-Juan Zhang, PhD

Xiamen University, Fujian, China

Ling-Juan Zhang, PhD, discussed the role of dermal fat in controlling neutrophil activity and inflammation in the skin. Dr. Zhang's research highlighted that neutrophils quickly infiltrate the skin in response to infection or danger signals. Still, excessive neutrophil accumulation can lead to chronic inflammation, as seen in generalized pustular psoriasis (GPP). Previously, dermal fat was shown to produce antimicrobial peptides combating bacterial infections.

Using a murine model, her team observed that mice developed significant skin inflammation by day six, followed by a phase of inflammation tolerance and regression of neutrophil recruitment from day six to ten. Further, single-cell RNA sequencing of mouse skin identified pro-inflammatory preadipocytes interacting with neutrophils. In vitro and in vivo studies confirmed that neutrophils release IL-1 β , activating preadipocytes and recruiting more neutrophils to the skin.

To validate these findings in humans, Dr. Zhang's team analyzed a published psoriasis single-cell RNA-seq database. They identified a similar pro-inflammatory preadipocyte population in humans, enriched with IL-1 signaling and associated with neutrophilic inflammation, particularly in GPP.

Prolonged activation of pro-inflammatory preadipocytes drives adipogenesis, forming new adipocytes that secrete anti-inflammatory molecules, resolving inflammation and restoring skin homeostasis. Dysregulation of this process might result in uncontrolled neutrophil accumulation in the skin, contributing to chronic inflammatory conditions.

Comparative Whole Metagenome Sequencing Analysis in Psoriasis Capitis Patients and Healthy Individuals

Britta De Pessemier

Ghent University, Ghent, Belgium

Psoriasis is an immune-mediated inflammatory disorder that significantly affects the scalp in 80% of patients, making it a challenging area to treat. Britta De Pessemier presented her research on the comparative genome analysis of the scalp microbiome in psoriasis patients versus healthy individuals.

The study collected 83 scalp samples from healthy individuals and 64 samples from psoriasis patients, performing DNA extractions and shotgun metagenomic sequencing. The data showed that lesional scalp areas in psoriasis patients had a significantly lower number of microbial reads and 16S copies compared to non-lesional areas and healthy scalps. This lower microbial biomass in lesional areas is attributed to increased human DNA due to keratinocyte turnover and higher amounts of antimicrobial peptides.

Further, lesional scalp areas are more dissimilar and contain fewer commensal species. The dominant microbial species in healthy scalps were *Cutibacterium* spp, particularly *Cutibacterium acnes*. However, lesional areas had fewer *Cutibacterium* species and more *Staphylococcus* and other species. Functional profiling revealed altered metabolic pathways in lesional areas, affecting substances (e.g., amino acids, carbohydrates, and lipids), potentially disrupting skin homeostasis and activating immune responses. Additionally, certain virulence factor genes, including those for antimicrobial resistance and biofilm formation, were enriched in lesional areas.

Britta de Pessemier emphasized that psoriasis lesions on the scalp exhibit a distinct and less diverse microbial community with fewer commensal species and altered functional potential, suggesting a significant role of the microbiome in psoriasis pathology. Brita de Pessemier's research opens new hypotheses for understanding and treating psoriasis, as audience questions highlighted the paradox of the finding of lower microbial biomass in psoriasis lesions compared to other studies.

Comparative Multiomics Study of Inflammatory Skin Diseases Uncover Novel Disease-Specific Heterogeneity in Skin Resident Myeloid Cells

Mehdi Rashighi, MD (on behalf of Khashir Abhashari, MD, MPH)

University of Massachusetts – Chan Medical School, Worcester, Massachusetts, United States

Mehdi Rashighi, MD, shared the presentation on behalf of Khashir Abhashari, MD, MPH, which focused on the heterogeneity of inflammatory skin diseases, including psoriasis. The study aimed to understand disease heterogeneity by conducting multi-omic studies on various inflammatory skin diseases and involved patients with psoriasis, vitiligo, cutaneous lupus erythematosus, and dermatomyositis. Suction blistering biopsies were used to obtain samples from lesional and non-lesional skin, including healthy controls. Single-cell RNA sequencing and high-throughput proteomics were also performed.

Results showed that the hierarchical clustering analysis distinguished the four diseases. In psoriasis, genes like IL-17 and IL-36 were elevated, as expected. Dermatomyositis and lupus showed strong type I interferon signatures at the RNA and protein levels. They also could distinguish diseases based on protein levels in interstitial skin fluid, reflecting RNA-level differences.

Focusing on single-cell resolution, the study identified disease-specific subsets of myeloid cells. Conventional DC2 cells were abundant in psoriasis, mediating IL-17 responses, consistent with high IL-17 levels in psoriasis lesions. Meanwhile, conventional DC1 cells were enriched in vitiligo lesions, crucial for cross-presenting antigens and activating CD8 T cells, which drive vitiligo.

These findings align with ongoing clinical trials targeting these pathways, highlighting the importance of disease-specific immune cell populations in developing targeted therapies.

Scaling Down Lung Disease: COPD Complications in Psoriasis Patients

Lily Guo, BS

David Geffen School of Medicine at the University of California, Los Angeles, United States

Lily Guo, BS, presented a retrospective cohort study using Optum's Clinformatics Data Mart Database (2007-2023) to determine the association between psoriasis and pulmonary disease. They compared pulmonary complications and all-cause mortality in patients with co-morbid psoriasis and chronic obstructive pulmonary disease (COPD) to those with COPD alone. Patients with co-morbid psoriasis and COPD had an increased risk of all pulmonary and acute pulmonary complications compared to those with COPD alone. However, patients with psoriasis had lower associations of chronic pulmonary complications such as pulmonary hypertension and respiratory failure. Patients with psoriasis and COPD also had lower mortality compared to patients with COPD alone. Patients with psoriasis and COPD may benefit from differential healthcare utilization and disease modification with systemic immunoregulatory medications. Although the authors controlled for smoking, patients with psoriasis have a higher prevalence of cigarette smoking compared to the general population.¹ More research is needed to determine the interplay between smoking, COPD, and psoriasis.

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Protective Effects of Apremilast Against Cardiovascular Disease in Psoriasis and the Role of Monocytes

Alison Treichel, MD, 2024 IPC Fellow

University Hospitals, Cleveland, Ohio, United States

Alison Treichel, MD, shared the cardioprotective effects of apremilast, a phosphodiesterase-4 (PDE-4) inhibitor, in patients with psoriasis. Psoriasis is known to cause systemic inflammation and is associated with cardiovascular disease (CVD). However, the role of systemic therapy on psoriasis is still being elucidated. The study aimed to determine 1) whether PDE-4 inhibition decreases the relative risk (RR) of CVD and 2) the mechanism using differential gene expression, specifically in CD14+ monocytes.

Dr. Treichel shared a retrospective cohort study that used the TriNetX database of over 600,000 patients to compare CVD outcomes over five years in psoriasis patients who received apremilast versus those who received only topical corticoid steroids (TCS). The study compared 8,364 patients in the apremilast and 8,364 patients in the control arm. Patients who received apremilast had a lower RR of heart failure (RR 0.71; confidence interval (CI) 0.59-0.84), myocardial infarction (RR 0.63; CI 0.63-0.87), cerebral vascular disease (RR 0.51; CI 0.46-0.73), deep vein thrombosis (RR 0.73; CI 0.63-0.97), hypertension (RR 0.71; CI 0.64-0.79). Patients treated with apremilast also had low-density lipoprotein lab values lower than those receiving TCS. Dr. Treichel later discussed a prospective cohort study that performed transcriptomic analysis on CD14+ monocytes from 14 patients treated with apremilast. Regulated pathways involved in monocyte activation included NADPH oxidase complex, vesicle fusion, and lipoprotein clearance. Overall, apremilast can improve psoriasis and cardiovascular outcomes by modulating systemic inflammatory responses mediated by monocytes.

Identifying Disparities in Phototherapy Dosing and Research Participation Among Patients with Psoriasis by Race, Ethnicity, and Skin Phototype: Findings from the Light Treatment Effectiveness Study

William Song, BS

University of Pennsylvania, Philadelphia, Pennsylvania, United States

William Song, BS, shared research that examined how narrow-band ultraviolet (NB-UV) phototherapy dosing and research participation among psoriasis patients differed by race, ethnicity, and skin type. This research is significant as patients with skin of color have more severe psoriasis and may be less likely to be prescribed biologics.¹ Data was extracted from the Light Treatment Effectiveness (LITE) study, a randomized pragmatic trial comparing office vs home phototherapy for psoriasis. The pragmatic trial had broad inclusion criteria to be generalizable to clinical practice and had 783 patients from 42 clinical sites. Overall, the study found that at-home phototherapy was not inferior to in-office phototherapy. Patients were stratified by Fitzpatrick skin phototypes. The number of patients per skin phototype was 350 with type I-II, 350 with type III-IV, and 83 with type V-VI. They found that patients with type III-VI skin were underdosed compared to skin types I-II ($p < 0.001$).

Additionally, 254 patients who declined to participate in the study were surveyed, of which 61% were White, 15% were Black, and 8% were Asian American or Pacific Islander. Among all patients who did not participate in the study, logistical barriers, lack of research interest, and financial factors were cited as important. Work schedule and distance to the phototherapy clinic were provided as examples of logistical obstacles. This study provides essential context regarding home vs. in-office phototherapy and barriers to care.

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Perceptions of Psoriasis Patients with BSA \leq 3% Not Being in Remission: Insights from the National Psoriasis Foundation Annual Survey

George Gondo, MA

National Psoriasis Foundation, Alexandria, Virginia, United States

New psoriasis medications have dramatically improved patient outcomes, but there is discordance between research clinician grading of remission and patient perspectives. Definitions of remission vary and include clinical scores such as the Psoriasis Assessment and Severity Index (PASI) and measurements of body surface area (BSA). Despite the clinical definition, patients with a BSA of involvement of less than 3% often do not self-report remission.

George Gondo, MA, shared a cross-sectional survey of patients with psoriasis that used the Patient Report of Extent of Psoriasis Involvement (PREPI), a validated patient-reported BSA outcome measure to survey patients. Patients with BSA \leq 3% were asked if they were in remission. Most (55.6%) psoriasis patients with a BSA of \leq 3% did not feel they were in remission. Patients who did not feel they were in remission were then asked to explain further. Explanations for this perception included persistent disease activity and symptoms. Patients further noted their long-term use of biologics, persistent pruritus/scaling, and involvement of sensitive areas such as the face and genitals. The overall theme of this research is that psoriasis is a chronic disease despite advances in therapy. Low disease activity with BSA \leq 3% does not represent true remission.

Effects of Systemic Biologic Treatments on Cardiovascular Outcomes Among Patients with Psoriasis

Jacky Chen, BS

University Hospitals Cleveland Medical Center, Cleveland, Ohio, United States

Chronic systemic inflammation from psoriasis drives cardiovascular disease (CVD) and decreased life expectancy.¹ It is unknown if patients receiving single-agent biologics have better outcomes. Jackie Chen, BS, used the TriNetX database to examine associations between CVD and psoriasis in patients taking a single-agent biologic over five years. Patients taking a TNF inhibitor, IL-12/23 inhibitor, or IL-17 inhibitor were compared to patients taking topical corticosteroids (TCS). The study did not directly compare the single-agent biologics against each other. The analysis excluded patients taking other systemic therapies and controlled for confounding variables such as age and comorbidities.

Patients taking TNF inhibitors had decreased relative risk (RR) of developing new-onset CVD compared to those taking TCS. TNF inhibitors were associated with reduced risk of myocardial infarction (RR: 0.30), acute coronary disease (RR:0.44), cerebral vascular disease (RR: 0.57), heart failure (RR:0.69), and atrial fibrillation (RR: 0.71). IL-17 and IL-12/23 inhibitors had decreased relative risk of heart failure alone compared to TCS. All three classes of biologics were also associated with lower serum cholesterol compared to TCS. One limitation is that the study could not assess social determinants of health, including economic stability, environment, and health care access. The study suggested that TNF inhibitors provide the greatest cardioprotective benefits compared to TCS.

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Paving a Path to Equity in Psoriasis

Junko Takeshita, MD, PhD, MSCE, IPC Councilor

University of Pennsylvania, Philadelphia, Pennsylvania, United States

Health disparities affect everyone, representing an approximately \$450 billion cost to the US health care system in 2018.¹ Junko Takeshita, MD, PhD, MSCE, gave the prestigious Eugene Farber Lecture. Dr. Takeshita focuses her career and research on equity in dermatology and how biases affect treatment and diagnosis. This is important as disparities can impact patient quality of life. Black, Asian, and Latinx patients with moderate to severe psoriasis have disproportionately affected quality of life compared to White patients.² Her approach centers on working with members of the communities.

During the presentation, Dr. Takeshita described patients' frustrations due to a lack of trust and poor communication. Some of these frustrations can result from doctors dealing with issues, including clinic delays, which limit patient time. Dr. Takeshita emphasized that understanding disparities and differences in care is essential to reducing biases when counseling patients. Dr. Takeshita provided a clinical example of treating hair conditions, including scalp psoriasis and seborrheic dermatitis, with prescription shampoos. She initially recommended washing her hair with shampoo two to three times per week. However, when Dr. Takeshita talked to her patients, she learned that frequent hair washing may be excessively damaging to Black patients. As a result, she now recommends using more oil vehicles, which require less frequent washing. In another example from her research, she cited how direct-to-consumer advertising for psoriasis biologics has underrepresented Black, Asian, and Latinx patients.³ This is significant as there are racial disparities in patient use and familiarity with biologics. Dr. Takeshita's presentation highlighted how research and shared decision-making can better characterize clinical disparities and increase equity of care.

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Identifying Barriers and Facilitators to Participating in Clinical Research Among Racial and Ethnic Minoritized Adults with Psoriasis

Veda Nagubandi

University of Pennsylvania, Philadelphia, Pennsylvania, United States

Previous research showed that White individuals are overrepresented in clinical trials.¹ As such, Veda Nagubandi examined the barriers to participation in clinical trials among underrepresented racial and minority groups. This was a qualitative study among 26 patients with psoriasis of Asian, Black, and Hispanic/Latinx origin with a median age of 48. Approximately two-thirds of the participants were female. The study had diverse representation from ethnic and racial groups: 38.5% Asian, 30.8% Black, and 30.8% Hispanic/Latinx.

The patients had never been involved in clinical trials at the time of the interview and were asked questions in a semi-structured interview. Two hypothetical studies were proposed involving either receiving treatment or providing tissue samples. Patients were asked about the significant barriers to participation in either of these hypothetical trials and what factors may facilitate participation in research. These hypothetical studies were modeled to represent a typical dermatology clinical or translational trial. Based on the responses, the barriers to clinical trial participation were identified, including logistics and lack of trust. For the drug intervention study, patients addressed safety concerns about adverse events. For the more invasive trial involving providing tissue biopsy samples, patients voiced concerns about scarring and the invasiveness of procedures. In addition, this study showed that factors that facilitate research participation include monetary compensation for time and effort, desire to help future generations, and understanding that diverse clinical trials can advance knowledge in underserved communities. This qualitative research sheds light on how future clinical trials can better enhance the design and increase diverse patient participation.

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Compensatory Role of Interleukin-17A in Regulating the Proliferation of Epidermal Keratinocytes in Psoriasis

Raghunath Chatterjee, PhD

Human Genetics Unit, Indian Statistical Institute, Kolkata, India

Raghunath Chatterjee, PhD, examined the interplay of genetics and dermatopathology in identifying the pathogenesis of psoriasis. Psoriasis involves both inflammation and keratinocyte hyperproliferation. This study sought to determine the mechanism of epidermal keratinocyte hyperplasia further. RNA and miRNA sequencing was performed on psoriatic and peri-lesional tissue. Transcriptomic analysis from tissue samples revealed that miRNAs are involved in epidermal hyperplasia. A miRNA, miR-7-5p, was upregulated in psoriatic tissue. *In vitro* studies sought further to analyze the effects of miR-7-5p on keratinocyte proliferation. In keratinocyte cell lines, overexpression of miR-7-5p decreased proliferation, while inhibition of miR-7-5p increased keratinocyte proliferation. The proposed mechanism is that IL-17 upregulates miR-7-5p, which subsequently targets the epidermal growth factor receptor (EGFR) and Leukemia inhibitory factor (LIF), a member of the IL-6 cytokine family. Previous research has shown that IL-17a is directly involved in keratinocyte proliferation through activation of EGFR.¹ As a result, miR-7-5p may be involved in a negative feedback loop and compensatory mechanism of IL-17. This study highlights the complexity of immune keratinocyte interactions and the role of positive and negative feedback loops.

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Predominantly Genital and Inverse Psoriasis (PGIP): Description of a Unique Psoriasis Subtype

Kathryn Haran, BS

University of California, San Francisco, San Francisco, California, United States

Kathryn Haran, BS, evaluated whether clinical subtypes of psoriasis that affect the flexural and genital surfaces are distinct from classical plaque psoriasis. This is significant as approximately 89-90% of patients have plaque psoriasis compared to 21-30% with genital and intertriginous involvement.^{1,2} For this research analysis, patients with inverse and genital psoriasis (less than 1% body surface area of plaque psoriasis) were grouped and termed "predominantly genitals and inverse psoriasis" (PGIP). The research hypothesis was that PGIP represents a distinct psoriasis phenotype with unique inheritance and demographics.

This study compared 25 patients with PGIP to 89 control patients with plaque psoriasis. Results showed that PGIP was associated with an older age of onset (38.8 years vs 28.6), a higher prevalence of joint disease (20% vs 10%), and a greater likelihood of nail involvement (40% vs 20%). However, PGIP was not as strongly associated with having a family history as plaque psoriasis. Genome-wide SNP typing demonstrated that PGIP had more genetic variants involving inflammation in the innate immune system. PGIP had a higher burden of polymorphisms at 77 non-HLA loci compared to plaque psoriasis. This research supports that patients with psoriasis affecting the genitals and inverse surface have unique prognoses and genetic factors from plaque psoriasis. Additional research is needed to determine whether PGIP has similar risk factors, comorbidities, and treatment as plaque psoriasis.

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