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as of March 2019
I would like to welcome you to the latest issue of the *IPC Psoriasis Review* newsletter, in which we have gathered important updates and educational resources for health care professionals who treat patients with psoriasis worldwide and scientists committed to psoriasis research innovation.

In this issue, we have included superb summaries and commentaries in our "Top 5" feature, which highlights important publications that advanced the field of psoriasis research in 2018. A second feature in this issue (see page 10) summarizes an important symposium presented by IPC’s Research Committee at the Society of Investigative Dermatology (SID) annual meeting this past May. The symposium brought together international thought leaders to discuss the intersection of psoriasis and cardiovascular disease.

I invite you to mark your calendars for 2 upcoming cutting-edge symposia, also developed by our Research Committee, which will be held later this year at the European Society of Dermatological Research (ESDR) and the Japanese Society of Investigative Dermatology (JSID) annual meetings. Discussions will focus on the adaptive and innate immune pathways of psoriasis and the mechanistic studies in plaque and pustular psoriasis, respectively. You can find additional details for these important programs on page 5.

IPC symposia discuss "hot topics" in psoriasis research and clinical care and include enlightening clinical case discussions. In this issue, you will find summaries of challenging cases focused on paediatrics, comorbidities, infections, and biologics taken from an IPC symposium presented at the Skin Inflammation and Psoriasis International Network (SPIN) meeting in Paris.

In the IPC News section, which begins on page 22, you will learn more about our advocacy efforts, recent publications, accomplishments of our volunteers, our symposium at the Reunión Anual de Dermatológos Latinoamericanos (RADLA) in Buenos Aires, and the exciting expansion of IPC’s Master Class program into the Middle East and Latin America.

I am pleased to report that behind the scenes, we have also been working hard on a new strategic plan to guide the organization in the coming years. IPC’s board members and councilors recently convened at the World Congress of Dermatology to identify and prioritize key initiatives, including access to care, personalized medicine, education, and global outreach. There is much work ahead, but we look forward to forging new partnerships, expanding our global network and presence, inspiring new leaders, and sharing the results of our efforts with you as we strive toward our vision of a world free of psoriasis. Thank you for being a part of our journey.

Very best wishes,

Jonathan Barker, MD, FRCP, FRCPath
President, International Psoriasis Council
1. Never-lesional skin in patients with mild psoriasis shows a disturbed microenvironment

A skewed pool of resident T cells triggers psoriasis-associated tissue responses in never-lesional skin from patients with psoriasis.


**SUMMARY**

Resident lesional T cells in moderate to severe psoriasis are well studied. Less is known about T cells in never-lesional skin from patients with mild psoriasis (NLP), investigated here by confocal imaging and flow cytometry. Tissue responses to T cell stimulation were furthermore measured by multiplex and NanoString technology. Interestingly, T cell activation ex vivo triggered psoriasiform and type I interferon tissue responses in NLP psoriasis. NLP-derived keratinocytes responded to IFN-γ stimulation with myxovirus 1 expression and IFN-α release. CCR6-expressing resident T cells producing IFN-γ and IL-17 were enriched in NLP-epidermis. Keratinocytes from NLP exposed to IL-17 and skin explants exposed to common fungal antigens responded with upregulation of the CCR6 ligand CCL20. Taken together, this implies that epidermal resident T cells capable of triggering psoriasiform tissue responses accumulate in NLP-epidermis. The interaction of the microbial microenvironment with genetically susceptible keratinocytes appears to shape the NLP T cells.

**COMMENTARY**

The microbial microenvironment has in the last years been one of the main interests in medicine, and psoriasis is not excluded from this trend. In order to investigate the early changes in the complex etiology of psoriasis, this study went not to the crowded place of T cells in the established plaque in moderate to severe psoriasis but tried to analyze the early events by focusing on never-lesional skin from patients with mild psoriasis. The clear disturbance of T cells and microenvironment described here encourages the search for therapeutic options that, following the intellectual concept behind the design of this study, might be able to interfere in these early subclinical stages of psoriasis or maybe even the microenvironment itself.

– Marcus Schmitt-Egenolf
2. Genetic markers may determine risk of developing psoriatic arthritis


SUMMARY

Psoriatic arthritis (PsA) occurs in about one-third of psoriasis patients. In this study, the authors use state-of-the-art statistical and machine-learning techniques to capitalize on the multitude of differences in the genetic architecture between PsA and cutaneous-only psoriasis (PsC) to predict the risk of developing PsA in the PsC population. The genetic data that populated their model were derived from 6 combined cohorts, resulting in 7,000 genotyped PsA and PsC patients. In their best predictions, the investigators achieved >90% precision with 100% specificity and 16% recall for predicting PsA among PsC patients, using conditional inference forest or shrinkage discriminant analysis, proving that genetic differences can potentially be used to predict PsA risk.

COMMENTARY

This study shows that despite the lack of a relevant single genetic marker for PsA, a multitude of markers can be employed to predict this risk with impressive precision. Given the fast development and diminishing analysis costs in the fields of genetics and machine learning, personalized diagnostics for PsA may well enter clinical praxis soon and inform treatment decisions. From a clinical point of view, it would be interesting to be able to predict the risk of PsA in advance of symptoms and signs in PsC patients. However, as physicians, we should remember that genetic-derived statistical risk prediction does not necessarily translate to real-world clinical risk. We should not see the disease course of the patient in front of us in a deterministic way. On the contrary, we should always encourage and empower our patients, as lifestyle decisions have a value both within and far beyond the treatment of psoriasis. – Marcus Schmitt-Egenolf

IPC’S RESEARCH COMMITTEE PRESENTS

Two upcoming scientific symposia

We invite you to learn more and pre-register to attend these important events at psoriasiscouncil.org/scientificsymposia

The mechanistic model(s) of psoriasis: Autoimmune and/or inflammatory?

Wednesday, September 18, 2019
49th European Society for Dermatological Research Meeting
Bordeaux, France
Program chairs: Michel Gilliet, Switzerland; Johann Gudjonsson, USA; Jörg Prinz, Germany
Program faculty: Chyung-Ru Wang, USA; Hervé Bachelez, France; Francesca Capon, UK

Dissecting psoriasis: Mechanistic studies in pustular and plaque psoriasis

Friday, November 8, 2019
44th Japanese Society for Investigative Dermatology
Aomori, Japan
Program Chairs: Jonathan Barker, UK; Christopher Griffiths, UK
Program faculty: Hervé Bachelez, France; Masamoto Murakami, Japan; Kazumitsu Sugiura, Japan

These programs are sponsored in part by Boehringer-Ingelheim
3. In phase 2 trial, oral agent BMS-986165, a TYK2 inhibitor, shows promise for treating psoriasis


SUMMARY

The strategy of identifying and targeting various key signaling pathways in psoriasis pathogenesis has been outstandingly successful in bringing powerful new therapies to benefit patients. Papp et al report on yet another approach, aiming at the enzyme tyrosinase kinase 2 (TYK2). Normally, TYK2 activates transcription (STAT)-dependent gene expression and activates functional responses of interleukin-12, interleukin-23, and type I and III interferon receptors. These pathways are involved in the pathogenesis of psoriasis and other immune-mediated disorders; hence, the logic of aiming at TYK2. BMS-986165 is the current catchy name of this latest creation from Bristol-Myers Squibb. It binds to the "pseudokinase" domain of TYK2, blocking further signal transduction. This study was a phase 2, double-blind trial, comparing 5 different dose regimens and one placebo group. As often in these early phase 2 studies, there were only 12 weeks of active therapy, with a 30-day follow-up. Randomization was stratified with respect to geographic region (Japan or the rest of the world), though the reason for this was not given. The study reported on a total of 267 patients. A Psoriasis Area and Severity Index (PASI) score of 75 was reached in 7% of the placebo group, 9% of the lowest-dose group (3 mg per day), and 75% of the highest-dose group (12 mg per day). There was a clear relationship between dose and effectiveness. There were 3 serious adverse events in patients receiving the active drug, as well as 1 case of malignant melanoma 96 days after the start of treatment. Eight patients (3%) developed mild to moderate acne and 12 (4.5%) reported diarrhea.

COMMENTARY

Results of this study showed that in the highest-dose group, which had an average age of 47 years, 4 out of 44 patients developed mild to moderate acne. The authors speculate that this could be due to the inhibition of cytokines involved in resistance to these organisms, resulting in proliferation of commensal bacteria and inflammation in the pilosebaceous units. Or, it might be chance. At the highest-dose investigated, 12 mg daily, 75% of 44 patients reached a 75% reduction in PASI and 64% reached a Dermatology Life Quality Index (DLQI)" score of 0 or 1. This sounds very promising, especially for a drug taken by mouth, but as the authors cautiously conclude: Safety and durability of effect remain to be determined. And this highest-dose group experienced the highest percentage of adverse effects.

Note: A recent article in the British Journal of Dermatology praised the New England Journal of Medicine for most often reporting confidence intervals (CIs) rather than p values in dermatology reports.¹ The gist of that BJD article was to encourage wider reporting of CIs by researchers to improve clinical interpretation of study results. So, it’s disappointing that in this NEJM article about TYK2, p values are given prominence. CIs provide a range in which the true value lies with a certain degree of probability as well as the strength and direction of the effect. So, statistical plausibility and clinical relevance of the study can be inferred. Admittedly, p values may appear to be clearer, but the 2 methods are complementary.

It was good to see that the investigators correctly defined the use of a “handprint” rather than a “palm,” as approximately 1% of body surface area. I admit I am biased over this, having struggled (mostly unsuccessfully) to help people understand this often wrongly or imprecisely defined concept. – Andrew Y. Finlay


¹ Dr. Finlay is joint copyright owner of the DLQI. He and Cardiff University receive royalties.
4. Study probes clinical and genetic differences in pustular psoriasis group of skin disorders


SUMMARY

Pustular psoriasis can be defined as the heterogenous family of pustular skin diseases that are associated with psoriasis vulgaris (PV). According to this generous definition of pustular psoriasis, even palmoplantar pustulosis (PPP) is included. Mutations in the IL36RN and AP1S3 genes have been described in this group. Pustular psoriasis manifests with repeated eruptions of neutrophil-filled pustules. The most severe form of this condition is generalized pustular psoriasis (GPP). Acrodermatitis continua of Hallopeau (ACH) affects the tips of fingers and toes and palmoplantar pustulosis (PPP) affects the palms and soles. In this study, the clinical and genetic features of pustular psoriasis were investigated by the analysis of an extended patient cohort. A total of 863 unrelated patients with pustular psoriasis were clinically investigated (GPP=251, PPP=560, ACH=28, multiple diagnoses=24). Psoriasis vulgaris occurred in about half of patients with GPP or ACH (54% GPP; 46% ACH) but only in 16% of PPP cases. The percentage of female patients was greater in PPP (77%) than in GPP (63%); likewise, the percentage of smokers was greater in PPP (80%) than in GPP (28%). GPP patients had the lowest mean onset age, 31 years (PPP 44 years and ACH 52 years). Mutation screening was performed in a subset of this cohort comprising 475 patients. IL36RN disease alleles were associated with earlier age of onset in all subtypes (P=0.003). IL36RN mutations were more common in GPP patients (0.19) and ACH patients (0.16) compared to PPP patients (0.03). AP1S3 alleles had similar frequency (0.03 - 0.05) across disease subtypes.

COMMENTARY

This is an important study, as the rarity of generalized pustular psoriasis and acrodermatitis continua of Hallopeau has previously limited this kind of combined genetic and clinical analysis across the extended pustular psoriasis family. This study underlines the clinical and genetic differences between PPP on the one hand and GPP and ACH on the other. Facts such as the comparatively weak association of PPP with psoriasis vulgaris and its strong association with smoking has earlier led to the conclusion that PPP should be separated from the psoriasis family and be seen as a unique entity on its own. This genetic investigation does not enlighten us on this question. IL36RN disease alleles were associated with earlier age of onset in all subtypes, pointing toward a disease-promoting function. However, the relative rarity of IL36RN mutations among patients with PPP may imply that future treatments with IL36 inhibitors are more likely to be therapeutically relevant in the group of GPP and ACH patients.

In March 2019, the first-in-class investigational treatment with the monoclonal antibody BI 655130 against the interleukin-36 receptor was published in The New England Journal of Medicine.1 In this proof-of-concept study, 7 GPP patients were treated with a single, open-label, intravenous dose. Only 3 patients carried the IL36RN mutation. The pustules were completely cleared in 6 patients by week two. The efficacy of BI 655130 regardless of the presence of the IL36RN mutation suggests that the interleukin-36 pathway may play a pathogenic role among patients with generalized pustular psoriasis with different genetic backgrounds, including those without target mutations. This could imply that IL36RN screening before treatment is not necessary. – Marcus Schmitt-Egenolf

5. Risankizumab shows superior effectiveness in treating moderate to severe psoriasis when compared with ustekinumab in phase 3 trials


SUMMARY

Risankizumab is a humanized IgG1 monoclonal antibody that binds to the p19 subunit of interleukin-23. It therefore inhibits this cytokine, which plays a key role in psoriatic inflammation. The aim of this study was to compare the efficacy and safety of risankizumab with placebo and with ustekinumab in moderate to severe chronic plaque psoriasis. Two replicate, multi-center, phase 3 studies across 14 countries involved 506 and 491 patients who were randomly assigned (3:1:1) to risakizumab 150 mg, ustekinumab 45 or 90 mg, or placebo for the initial double-blind 16 weeks. At week 16, the placebo group switched to risankizumab and the other patients continued on their original drug up to week 52. A Psoriasis Area and Severity Index (PASI) score of 90 was achieved at 16 weeks by 75.3% in the first study and 74.8% in the second study of patients on risakizumab, by 42% and 47.5% respectively, of patients on ustekinumab, and by 4.9% and 2.0% of patients on placebo. Confidence intervals were reported and demonstrated clear differences between the treatment groups. Secondary outcome measures included the Dermatology Life Quality Index (DLQI)* and the Psoriasis Symptom Scale (PSS), which scores the severity of pain, redness, itching, and burning. A DLQI score of 0 or 1 was achieved at week 16 by 66% and 67% of patients on risakizumab, by 43% and 46% on ustekinumab, and by 8% and 4% patients on placebo. A PSS score of 0 was achieved at 16 weeks by 29% and 31% of patients on risakizumab, 15% and 15% patients on ustekinumab, and 2% and 0% patients on placebo. Treatment-emergent adverse events were similar across patients treated with risakizumab, ustekinumab, and placebo.

COMMENTARY

This is another well-organized and well-reported study adding major new evidence of the outstanding effectiveness of risankizumab and of superior effectiveness compared to ustekinumab. Interleukin- (IL-) 23 drives the development of psoriasis by stimulating T-helper-17 and innate immunity cells, which are major sources of pro-inflammatory cytokines. Whereas ustekinumab blocks the p40 subunit that both IL-12 and IL-23 share, risankizumab targets the p19 subunit, specific for only IL-23. The study is notable and especially valuable clinically, as it is one of the very few major studies to directly compare, head-to-head, two biologics with differing modes of action. Clinicians are now overwhelmed with choice of biologics for psoriasis, all providing greater benefit than our previous systemics. For each, the evidence of individual effectiveness may be clear, but the clinician needs to know how they directly compare: We need many more similar head-to-head studies. Pharmaceutical companies Boehringer Ingelheim and AbbVie closely cooperated over this study: Boehringer Ingelheim had sold the commercialization rights of risankizumab to AbbVie in 2016. It is not stated whether the maker of ustekinumab was involved in the study. The baseline demographics table reveals that 72% of the 996 patients weighed >100kg, regrettably reflecting accurately the reality of this comorbidity in patients with severe psoriasis. However, the ethnic origin of study participants in these international studies was 78% white, 17% Asian and only 1.6% black or African-American. This raises the general broader question of what steps clinical study organizers take to ensure recruitment of an appropriate racial mix.

– Andrew Y. Finlay

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By Thomas Scharnitz, MD

Dr. Scharnitz received his medical degree from Pennsylvania State University and completed his intern year in internal medicine at the University of Virginia. He is currently in his third year of training as a resident physician at the University of Michigan Department of Dermatology.

Recent research has made significant advances in understanding the link between cardiovascular disease and psoriasis. That association was the focus of a symposium presented by IPC’s Research Committee at the Society for Investigative Dermatology (SID) meeting in Chicago, Illinois, in early May. Discussions explored mechanistic models, epidemiological data, imaging studies, and immuno-intervention strategies for this complex scenario.

Co-chairs for the program – entitled, “Cardiovascular disease in psoriasis: A changing paradigm” – were IPC Councilors April Armstrong, University of Southern California, Los Angeles, California, United States; Johann Gudjonsson, University of Michigan, Ann Arbor, Michigan, United States; and Nehal Mehta, National Heart, Lung and Blood Institute, Bethesda, Maryland, United States.

Part 1 of the symposium featured 5 faculty presentations, with expert-led panel discussions. Part 2 included a 1-hour session featuring a series of selected poster presentations that provided additional insights into disease mechanisms that contribute to psoriasis and its comorbidities.

**PART ONE: LECTURES**

**Immunopathogenesis of atherosclerotic disease: Where are we now?**

*Dr. Hafid Ait-Oufella, a cardiologist and PhD in immunology at Université Paris Descartes, began the symposium with a discussion on the immunopathogenesis of atherosclerotic disease. He described the role of both innate and adaptive immunity as a “delicate balance” between atherogenesis and atheroprotection.*

Innate immunity in atherosclerosis is well established. Smith et al demonstrated that macrophage-deficient mice form no atherosclerosis.1 Furthermore, Varghese et al demonstrated 30% plaque reduction in IL-1β knockout mice.2 Ridker et al showed significant protection (lower rate of recurrent cardiovascular events) with canakinumab in patients who previously experienced myocardial infarction and had persistent chronic low-grade inflammation (CRPus>2mg/l).3 With TNF-α inhibitors, patients with psoriatic arthritis showed 50% reduction in atherosclerotic plaque development as measured by ultrasonography in the carotid artery and reduced cardiovascular events in patients with severe psoriasis.45

The role of adaptive immunity in atherosclerotic disease is more recently described. Zhou et al demonstrated that CD4(+) T cells promote atherosclerosis in mice, and Whitman et al demonstrated the vigorous pro-atherogenic role of TH1-derived IFN-γ.67 Conversely, Dr. Ait-Oufella had identified the protective role of...
a subset of CD4+ T cells called natural regulatory T cells through several mechanisms, including IL-10 and TGF-beta production.8

Importantly, relating to psoriasis, the role of Th17 remains controversial. Some experimental studies suggest atheroprotection during IL-17 blockade, whereas others suggest atherogenesis.3,10 In acute coronary syndrome patients, high plasma IL-17 level is associated with better cardiovascular outcome.11 Dr. Ait-Oufella believes that the vascular impact of IL-17 may depend on global cytokine environment, being protective in IL-10-rich conditions but pro-atherogenic in the case of high concomitant production of IFN-γ, evidenced in studies by Taleb.12

Epidemiology of cardiovascular disease in psoriasis

In an informative and practical lecture, IPC Councilor April Armstrong, professor and associate dean at the University of Southern California, explored the epidemiologic relationship between psoriasis and cardiovascular disease.

She discussed study characteristics, data collection, and aspects of epidemiologic research, including the strengths and weaknesses of the various study types, biases, and criteria for real association. She also focused on confounding, which is especially important between psoriasis and common cardiovascular risk factors and comorbidities. Dr. Armstrong subsequently summarized several meta-analyses, evaluating associations between psoriasis and multiple comorbidities, namely obesity, diabetes, hypertension, and the metabolic syndrome.

Regarding diabetes, Dr. Armstrong’s group demonstrated increased overall odds ratio (OR, 1.59) and “severity stratified” pooled ORs (mild, 1.53 and severe, 1.97) in patients with psoriasis compared to controls.13 Regarding obesity, they found increased overall OR (1.66), and pooled ORs (mild, 1.46 and severe, 2.23).14 This association appears even stronger in the psoriatic pediatric population, as shown in a study by IPC Councilor Amy Paller, which displayed increased overall OR (4.29) and pooled OR (mild, 3.6 and severe, 4.9).15 Regarding hypertension, they found increased overall OR 1.58.16 Finally, regarding the metabolic syndrome, Dr. Armstrong’s group found increased overall OR (2.26) and pooled ORs (mild, 1.56, severe, 1.98), though she noted funnel plots demonstrated substantial publication bias.17 Dyslipidemia data are lacking due to varied nomenclature and coding.

Importantly, Dr. Armstrong discussed findings from several well-conducted epidemiologic studies where no association was revealed between psoriasis and cardiovascular risk factors and events. Notably, Parisi et al, examining the CPRD database, showed no association between severe psoriasis and major adverse cardiovascular events (MACE) after adjusting for confounders.18 She noted that the Parisi study had several strengths in rigorous identification of cohorts, modeling of risk factors that accounted for development of new risk factors over time, and using severity of psoriasis as a time-varying covariate. Given the conflicting study findings from prior literature, it remains an evolving story regarding the association between psoriasis and cardiovascular risk factors and outcomes.

In closing, Dr. Armstrong emphasized the importance of accurate identification of cohorts, careful adjustment for confounders, the need to model for development of new comorbidities over time, and accounting for inflammatory arthritis in epidemiological studies in order to maximize validity of the findings.

Is psoriasis an independent risk factor for cardiovascular ischemic disease?

Marlies Wakkee, dermatologist at the Erasmus University Medical Center Rotterdam, the Netherlands, presented an informative discussion examining studies that reported the association of psoriasis as an independent risk factor for ischemic heart disease (IHD).

The first studies describing an association between psoriasis and cardiovascular (CV) events date back more than 40 years. In 2006, IPC Councilor Joel Gelfand of the University of Pennsylvania published a landmark paper in the Journal of the American Medical Association positioning psoriasis as an independent risk factor for myocardial infarction.19 Since then, many studies have examined this association. Notably, a meta-analysis further demonstrated increased risk of IHD in psoriasis, but population-based data did not show significant associations.20 This is likely because, to date, most studies are observational, based on secondary databases, and, therefore, are not designed to investigate the causal relationship between psoriasis and IHD and confer significant risk of detection bias.

Dr. Wakkee’s group highlighted detection bias in an observational study in which regular office visits for psoriasis subsequently led to increases in both comorbidity diagnoses and medications administration.21 Furthermore, the large population-based cohort Rotterdam Study, which minimized detection bias, failed to demonstrate increased risk of IHD in both mild and severe psoriasis.22 Residual confounding also complicates observational studies, as Egeberg et al demonstrated a role for family history in this association. This study showed that only those patients with psoriasis with family history of cardiovascular disease exhibited a personal increased risk of CV events.23
Dr. Wakkee concluded that, based on observational studies, there is at least a complex association between psoriasis and IHD, but at this time it remains unclear if psoriasis is an independent risk factor. Future studies investigating the effect of systemic therapies on the risk of IHD in patients with psoriasis will be highly interesting to further elucidate this association.

**In vivo studies of cardiovascular disease in psoriasis: An update**

IPC Councilor Nehal Mehta, who heads the Laboratory of Inflammation and Cardiometabolic Diseases at the National Heart, Lung and Blood Institute in Bethesda, Maryland, presented vast in vivo data on the pathogenesis and therapeutic interventions on atherosclerotic plaques and cardiovascular disease (CVD) in psoriasis.

Dr. Mehta first discussed atherogenesis in which high-risk lesions ultimately rupture and cause acute coronary syndrome (ACS). In unpublished data, his group discovered that psoriasis yields 9-fold elevation in TNF-α and 5-fold elevation in IL-1β during troponin-positive ACS. Additionally, psoriasis is associated with atherogenic lipid composition with an increase in apolipoprotein B lipoproteins and also reduced function of HDL as measured by HDL cholesterol efflux capacity.

Using FDG-PET (fluorodeoxyglucose positron emission tomography), Dr. Mehta’s group found that psoriasis severity correlates with aortic inflammation. This inflammatory level mirrors nonpsoriasis patients with known CVD. Furthermore, there are more coronary plaques that occur nearly 10-15 years sooner in psoriasis. Last year, using quantitative coronary angiography, Dr. Mehta also highlighted increases in total plaque burden in psoriasis, 95% of which is noncalcified (high risk) and rupture prone.

Most recently, his group completed an observational study in which 121 biologic-naïve psoriasis patients (moderate-severe) who received biologics (n=89) were compared to those who did not (n=32). At 1 year, patients on biologics had reduction in necrotic core (-57%, p=0.09), and both total (-5%, p=0.009) and non-calcified (-6%, p=0.005) plaques. In subgroup analysis, significant reductions in noncalcified plaques occurred with both anti-TNF (6%, p =0.06, n=48) and anti-IL17 (15%, p=0.005, n=22) treatment groups.

Dr. Mehta concluded that biologics may curtail these psoriasis-driven inflammatory CVD phenotypes, but randomized controlled trials are necessary to validate the evidence.

**Effect of psoriasis treatment on cardiovascular risk: Reconciling clinical trials and observational studies**

In an interactive question-and-answer lecture, IPC Councilor Joel Gelfand, dermatology professor/researcher at the University of Pennsylvania, discussed the importance of critical evaluation of the literature. Substantial evidence exists to show that patients with psoriasis have an increased risk for major cardiovascular events and mortality, with the risk being most significant in patients who require systemic or phototherapy or have >10% body surface area affected. Recent guidelines from the American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF), the American Heart Association (AHA) and the American College of Cardiology (ACC) recognize the importance of CV risk in patients with psoriasis, and advocate for more aggressive management of cholesterol levels as one approach to mitigating this risk.

A logical hypothesis is that treatment of psoriasis is associated with a lowering of CV disease and mortality. A variety of studies have demonstrated that both methotrexate and TNF inhibitors are associated with a decreased risk of CV events in patients with rheumatoid arthritis or psoriasis. Recent work by Margolis and Gelfand (J Am Acad Dermatol 2019), however, has demonstrated a strong healthy-user effect for psoriasis patients treated with biologics. Thus it remains uncertain whether the reduction of CV events seen in observational studies is a drug effect or the healthy-user effect. Similarly, Gelfand showed data from the VIP (Vascular Inflammation in Psoriasis) trials and compared them to observation data and demonstrated the importance of placebo control in interpreting biomarker studies.

Recently and for the first time, clinical trials evaluated the impact of immune-targeted treatments on CV events as a measure of secondary prevention (ie, all patients in these trials have established coronary artery disease). CANTOS, a study of canakinumab, a biologic that blocks IL-1β, demonstrated clear proof of principle that a targeted biologic can lower the risk of CV events. However, the Cardiovascular Inflammation Reduction Trial (CIRT), a randomized placebo-controlled study of methotrexate, failed to demonstrate any benefit of the drug on CV events in patients with established coronary artery disease. In contrast to CANTOS, patients in CIRT were not required to have elevated C-reactive protein (CRP) and, thus, had no evidence of residual CV risk related to inflammation. Therefore, it seems likely that if methotrexate were studied in an inflamed population (ie, patients with rheumatoid arthritis, psoriasis, or coronary artery disease with elevated CRP), CIRT would have yielded results similar to CANTOS and observational studies of methotrexate.
In summary, Dr. Gelfand emphasized that practitioners must act on the data they currently have and do a better job of educating, screening, and treating modifiable cardiovascular risk factors. Fortunately, psoriasis’s role in cardiovascular disease is becoming more widely accepted, and joint guidelines issued by the AAD-NPF and by the ACA-AHA now recognize its importance in CVD intervention.26,27

PART TWO: POSTER PRESENTATIONS

Trans-disease meta-analysis between psoriasis and type 2 diabetes reveals shared genetic signals.

Matthew Patrick, PhD, University of Michigan, Ann Arbor, Michigan, United States

- Published studies suggest that psoriasis and type 2 diabetes (T2D) are significantly associated. This study performed large-scale trans-disease meta-analysis using previous association studies for psoriasis (11,024 cases, 16,336 controls) and T2D adjusted for BMI (74,124 cases, 824,006 controls), utilizing 8,016,731 well-imputed markers from both diseases.
- The study identified 11 loci with shared direction of effect, including 4 that exhibited suggestively significant p-values (p<1x10^-4) in both diseases.
- Among these loci, the chromosome 2 signal rs840967 (p=9.6 x 10^-9, psoriasis OR=1.08, T2D OR=1.04) is in proximity to a shared locus (2p14) for multiple chronic inflammatory conditions, and rs840967 is an expression quantitative trait loci (eQTL) in whole blood for SPRED2 (p=8.3x10^-27), an inhibitor of MAP kinases.
- Together with the 3 other trans-disease loci (10q24.31, 11q13.1 and 17q21.2) encompassing CHUK, PRDX5 and STAT3, respectively, results indicate the shared disease loci include common transcripts that participate in NFkB and other immune cascade signaling.
- Interestingly, only one of the shared loci (11q13.1) is in linkage disequilibrium (D’=0.81) with previously identified signals for BMI.
- Conclusion: The results highlight potentially BMI-independent genetic links shared between psoriasis and T2D, and can ultimately help guide future research aimed at treating both conditions.

The adaptor protein Act1 plays a key role in psoriatic inflammation mediated by IL-23.

Alex Lipovsky, PhD, AbbVie, Worcester, Massachusetts, United States

- Act1 is an intracellular adaptor protein and a putative ubiquitin E3 ligase. Silencing of Act1 expression in human keratinocytes and fibroblasts blocks pro-inflammatory cytokine secretion induced by IL-17.
- In this study, Act1 knockout mice were resistant to increases in CXCL1 plasma levels induced by subcutaneous injection of recombinant IL-17A. These Act1 knockout mice were also protected against psoriasiform changes, gene expression for antimicrobial peptides and chemokines, and infiltration of immune cells after injection of IL-23.
- The L286G mutation was previously suggested to compromise Act1 ligase function and inhibit IL-17 signaling. Act1 “L286G knock-in” mice were susceptible to both IL-23 and IL-17 inflammatory effects.
- Primary Act1 “L286G knock-in” mouse fibroblasts, as well as human Act1 knockout fibroblasts reconstituted with a homologous point mutant, responded normally to IL-17 stimulation (unchanged from wild type).
- Conclusion: This study highlights the critical contribution of Act1 to proinflammatory skin changes mediated by the IL-23/IL-17 signaling axis.

XCL10 expression is regulated by keratinocyte STAT3 signaling and inhibits skin inflammation.

Nate Archer, PhD, Johns Hopkins School of Medicine, Baltimore, Maryland, United States

- The role of STAT3 signaling in psoriasis is not entirely clear. This study evaluated the relative contribution of STAT3 in keratinocytes (KCs) versus T cells in the imiquimod mouse model, using cre/lox mice with either KC inducible deletion of STAT3 (K5-STAT3), or specific deletion of STAT3 in T cells (Lck-STAT3).
- Unexpectedly, psoriasiform skin inflammation was diminished in K5-STAT3 mice, whereas Lck-STAT3 mice developed wild-type-like (wt) psoriasiform inflammation.
- K5-STAT3 mice also had increased IFN-γ+ T cells but less IL-17+ T cells compared to wt-mice. This suggested loss of STAT3 signaling in KCs dampened inflammation by inhibiting IL-17 responses while promoting IFN-γ responses.
mRNA and histologic expression of CXCL10 inversely correlated with the skin inflammation in deletion (K5-STAT3 mice) or overexpression (STAT3 overexpressed mice, KC14-stat3) of STAT3.

Neutralizing CXCL10 signaling enhanced imiquimod-induced skin inflammation, suggesting that CXCL10 acts to inhibit skin inflammation in this model.

Conclusion: The findings define a novel mechanism by which KC, but not T cell-intrinsic, STAT3 signaling induces psoriasiform inflammation via regulation of CXCL10 expression, proinflammatory IL-17, and anti-inflammatory IFN-γ T cell responses.

Targeting chemokine receptors CCR6 and CXCR2 in a murine model of IL-36α-induced pustular psoriasis.

Karen Ebsworth, BSc, ChemoCentryx, Mountain View, California, United States

Generalized pustular psoriasis (GPP) is linked to loss-of-function mutations in the gene encoding IL-36RA, an important negative regulator of IL-36 signaling.

In this murine model, intradermal injections of pre-activated IL-36α caused markedly increased total skin and epidermal thickness, and increased concentrations of CCR6 and CXCR2 and accumulations of various inflammatory cells.

The accumulated inflammatory subsets in IL-36α-treated skin all expressed either CCR6 or CXCR2 to some extent.

“CCX624”, an orally bioavailable small molecule CCR6/CXCR2 antagonist, reversed inflammatory cell accumulation and decreased both skin and epidermal thickness. CCX624 was effective in both prophylactic and therapeutic dosing regimens, and was more effective than saturating doses of both anti-TNFα and anti-IL17RA.

Conclusion: This study suggests CCR6 and CXCR2 are novel targets for inflammatory skin diseases involving dysregulated IL-36 signaling, such as GPP.

Comparing RNAseq analysis of the mouse IL-23 minicircle model to human psoriasis and other preclinical models of skin inflammation.

Laura Leys, BS, AbbVie, North Chicago, Illinois, United States

Hydrodynamic delivery of a single IV injection of IL-23 minicircles (MC) in mice induces psoriasiform dermatitis and elevates key IL-23/IL-17 pathway cytokines/chemokines.

In the study, RNAseq analyses from MC mice revealed that 15 of the top 20 affected pathways were also amongst the top 20 pathways identified in human psoriasis (Li et al, 2014) including those related to the IL-17A/F pathways.

Though both IL-23 models (MC and imiquimod) show the strongest alignment to human psoriasis, the MC model tended to have a more amplified RNAseq signal. Most upstream regulators were shared between human psoriasis and the MC model.

Treatment with apremilast, as well as anti-IL-23p40, anti-IL-23p19, or anti-TNF mAbs suppressed most of the gene changes in the MC model.

Conclusion: The study demonstrates that both IL-23 models align closely with human psoriasis, but the IL-23 MC tends to have a more amplified signal of these key pathways.

Depletion of the microbiome using broad-spectrum antibiotic cocktail improves the psoriasiform phenotype via attenuation of TNFα and IL-23-IL-17A in three psoriasis mouse models.

Jessica Ludwig, MSc, Case Western Reserve University, Cleveland, Ohio, United States

The potential contribution of the microbiome in psoriasis remains unclear. In this study, KC-Tie2, IL-17C+, and KLK6+ psoriasiform mouse models were treated with a broad-spectrum antibiotic cocktail.

Compared to controls, antibiotic-treated IL-17C+ and KLK6+ mice each demonstrated a 41% decrease in acanthosis (P<0.001). KC-Tie2 mice showed no improvement in acanthosis, but treatment did lengthen the time to thrombus formation by 75% in an experimental assay in the KC-Tie2 mice.

Using quantitative RT-PCR of signature psoriasis transcripts, antibiotic-treatment decreased the following cytokines:
- KLK6+ mice decreased TNFα (75%, P=0.02) and IL-23 (59%, P=0.004)
- IL-17C+ mice decreased IL-17A to undetectable levels (P<0.001)
- KC-Tie2 mice decreased TNFα (33%, P=0.05), IL-23 (41%, P=0.05) and IL-17A (51%, P=0.07).
- The decreases across all three models aligned with decreases in skin CD4 and CD8+ T cells, and CD11c+ and F4/80+ myeloid cells.
• Conclusion: The findings point to a key role for the microbiome in modulating the TNFα / IL-23 / IL-17A pathway in psoriasis. Further studies are ongoing.

Concerns about psoriasis differ by race: implications for patient-centered goal-setting and counseling.

Junko Takeshita, MD, PhD, MSCE, University of Pennsylvania, Philadelphia, Pennsylvania, United States

• Some data suggest that psoriasis may be more severe and have a greater negative quality-of-life impact on minorities, but little is known regarding the experience of, and concerns about, psoriasis among different racial/ethnic groups.

• This study performed semi-structured interviews of 68 individuals (white N=36, black N=32) with moderate to severe plaque psoriasis, assessing knowledge, experience, beliefs, and attitudes regarding psoriasis. Study characteristics were similar between white and black subjects.

• The team identified “concerns about psoriasis” as an important theme. Across all subjects, major themes included physical symptoms and aesthetic distress, ranging from visual unsightliness to social and emotional isolation.

• In particular, concerns about scarring and disease recurrence were prominent among blacks, whereas concerns about comorbid disease and heritability were prominent among whites.

• Conclusion: The study found that white and black patients with psoriasis had both shared and unique concerns about psoriasis, which is important in considering patient-specific goals and therapies.


Charlotte Read, MBBS, BSc, University of Southern California, Los Angeles, California, United States

• This study sought to determine the impact of mental health comorbidities on patients’ perception of patient-provider communication quality among U.S. adult patients with psoriasis, using validated instruments and adjusting for socio-demographics and comorbidities.

• The cross-sectional study used the Medical Expenditure Panel Survey (MEPS) data from 2003-2015. Among 7.35 million U.S. adult patients with psoriasis, 73% had no or mild psychological distress, 21% had moderate distress, and 6.0% had severe distress. Additionally, 91% had no or mild-to-moderate depression and 9.0% had severe depression.

• Compared to patients in a good mental health state:
– Patients with moderate or severe psychological distress were 4.2 times more likely to perceive low-quality patient-provider communication [OR: 4.23 (1.61-11.14); p= 0.004]
– Patients with moderate and severe depression were 4.6 times more likely to perceive low-quality patient-provider communication [OR: 4.59 (1.89-11.15); p= 0.001].

• Conclusion: Patients’ mental health state is associated with their perception of patient-provider communication, a key component of patient satisfaction.

REFERENCES
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Practical approaches to treating psoriasis were discussed through the lens of challenging cases at an IPC symposium presented during the Skin and Inflammation & Psoriasis International Network (SPIN) Congress in April in Paris, France. IPC Chief Medical Officer Peter van de Kerkhof, professor emeritus Radboud University, Nijmegen, the Netherlands, chaired the symposium, entitled “Challenging Cases in Psoriasis: A focus on pediatrics, comorbidities, infections, and biologics.”

Worsening of psoriasis under infliximab

In his lecture, IPC Councilor Errol Prens, Erasmus University Medical Center, Rotterdam, the Netherlands, presented a fascinating account of paradoxical manifestations to biologics in patients with immune-mediated disorders. Paradoxical reactions are defined as the new onset or exacerbation of a symptom/disease that usually improves with the biologic (TNF-α inhibitors).

Psoriasiform skin reactions are the most frequent and well-known paradoxical effects, but the list of other types is lengthy. They include autoimmune or autoinflammatory diseases such as lupus, uveitis, multiple sclerosis, vasculitis, sarcoidosis, hidradenitis suppurativa (HS), and Crohn’s disease.¹ The mechanisms underlying these paradoxical reactions are still a matter of debate. One possible mechanism involves an imbalance of cytokines favoring Type 1 interferons, chemokines, and possibly interleukin-(IL)-23/IL-17 and Tregs, together with underlying genetic factors. Most paradoxical reactions are caused by TNF-α inhibitors, but cases associated with ustekinumab, secukinumab, and ixekizumab have been documented.²

Professor Prens presented several cases of paradoxical reactions in patients with psoriasis, which included one case of worsening of the disease treated with infliximab. Most reactions clear upon discontinuation of the drug or by switching to another biologic. In some cases, additional therapies are required to manage the reaction. The underlying mechanisms, particularly genetic factors, require further research to identify patients at risk of developing paradoxical reactions.

Erythrodermic psoriasis and HIV infection

IPC Councilor Fernando Valenzuela, University of Chile, Santiago, Chile, discussed erythrodermic psoriasis, which is an uncommon, severe, inflammatory form of the disease.

Erythrodermic psoriasis usually manifests in patients with long-standing, unstable chronic disease. Triggering factors include HIV infection, emotional stress, intense ultraviolet light exposure, use of topical tar products, alcoholism, abrupt withdrawal of oral or topical corticosteroids, and methotrexate therapy. Erythrodermic psoriasis is associated with severe complications such as sepsis, acute kidney damage, respiratory distress, electrolyte imbalance, severe anemia, altered thermoregulation, protein depletion, and cardiac failure.³
Dr. Valenzuela presented an interesting case of a patient with a long history (50 years) of chronic mild psoriasis who then presented with dramatic worsening of psoriasis severity, fever, and weight loss. The patient tested positive for HIV infection. Psoriasis can appear as the first manifestation of HIV infection; therefore, HIV testing should be carried out in some new severe cases and in patients with sudden worsening of previously stable psoriasis, particularly in countries where HIV is prevalent. Psoriasis severity is proportional to the degree of immunosuppression, being most severe when CD4 counts <100 cells/mL. Even though HIV-associated psoriasis can present with any phenotype, erythrodermic, guttate, and acral psoriasis, as well as psoriatic arthritis tend to be more common. Treatment of moderate to severe HIV-associated psoriasis poses a therapeutic challenge, as most systemic treatments are immunosuppressive and could lead to severe complications. Anti-retroviral therapy, phototherapy (narrowband ultraviolet light B [UVBnb] or ultraviolet light A with psoralen [PUVA]) and oral retinoids are considered first treatment options.

Treatment-resistant psoriasis

Professor van de Kerkhof addressed the challenging topic of treatment-resistant psoriasis in a patient with contraindication to biologics due to active infection.

In his presentation, Professor van de Kerkhof discussed the case of a 75-year-old man with a 30-year history of classical chronic plaque psoriasis, with no signs or symptoms of arthritis or of metabolic syndrome/cardiovascular disease. After 20 years of mild involvement, during the subsequent 10 years, this patient presented with unstable phenotype that included remissions and exacerbations. Previous treatments with topical therapies had resulted in adequate control; however, during the next 10 years, he received several courses of UVB treatment, at times in combination with acitretin, with adequate control for approximately 2 years. He then received methotrexate, which was well tolerated but not effective to control symptoms, and he experienced remissions and exacerbations. The patient then started on a round of ciclosporin and within two weeks developed fever and generalized pustular psoriasis.

The pustular psoriasis diagnosis, with transition from plaque psoriasis to unstable psoriasis, should be regarded as psoriasis with pustulation. In fact, it is unstable psoriasis. This is different from pustular psoriasis with no transition into plaque psoriasis. The latter can be regarded as a distinct disease entity with a different genotype. In this patient, urinary tract infection with pyelonephritis and urosepsis was also diagnosed. The urinary tract condition remained an increased infection risk and constitutes the triggering factor.

Professor van der Kerkhof discussed to what extent all biologics are contraindicated in patients affected by infection. Recent analyses of the Psoriasis Longitudinal Assessment and Registry PSOLAR cohort (11,466 patients with psoriasis) suggested a higher risk of serious infection with adalimumab and infliximab, whereas, with ustekinumab and etanercept, no increased risk was observed. So far, active infection remains a contraindication for all biologics in published guidelines. Therefore, this patient was contraindicated for treatment with biologics.

Another finding in this patient was liver test abnormalities. The increases of transaminases occurred in this patient synchronously with exacerbations of psoriasis. In the literature, patients with unstable psoriasis and pustular psoriasis may have abnormal liver enzyme function independent from the medication and dependent on relapses of psoriasis.
**Psoriasis comorbidities**

In his presentation, IPC Councilor Ron Vender, Dermatrials Research Inc., Hamilton, Ontario, Canada, discussed the importance of addressing psoriasis comorbidities with the patient during clinic visits.

Patients with psoriasis often have comorbidities that can determine which biologic is best for them or which to avoid. Many psoriasis-related comorbidities are contraindications to traditional systemic medications as well.

Dr. Vender presented a case of a 54-year-old male patient with psoriasis who exhibited with many comorbidities, including obesity and depression. He was initially prescribed 300 mg of secukinumab at weeks 0-1-2-3-4, then 300 mg every 4 hours. The patient was quite pessimistic about treatment success, but his treatment response was as expected. However, continued clinical follow-up revealed a small amount of regression in his clinical response, and optimization of treatment was required by increasing the secukinumab dose at week 24 to 450 mg q 4. Importantly, his depression and depressive symptoms improved during his treatment, enhancing his quality of life with a reduction in DLQI to zero. This case can encourage dermatologists to take a “head-to-toe” treatment approach that would manage the signs and symptoms of psoriasis and also improve their patients’ quality of life.

**Pediatric psoriasis algorithm**

Nowadays, many effective and safe treatments are available to treat children and adolescents who have psoriasis, and many more will be approved soon. IPC Councilor Dr. Marieke Seyger, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands, presented a treatment algorithm that can be used as general guidance for the treating physician (Figure 1).

Despite the presence of the algorithm, however, managing the disease can be challenging. In order to personalize care in pediatric psoriasis, practitioners need to know patients’ values and preferences, but, particularly in adolescents, it can be difficult to glean this information. The use of the Children’s Dermatology Life Quality Index (CDLQI) is helpful. In addition, showing and discussing a graph of the patients’ quality of life (CDLQI) and severity of psoriasis (PASI) over time improves interactive consulting and facilitates shared decision-making.

Another challenge is determining which children should be treated with systemic treatments at an earlier stage and if they are at

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**Figure 1: Management of pediatric psoriasis**

| Corticosteroids/vit D analogues (two-compound) | In facial/flexural psoriasis optional: |
| Dithranol | Calcineurin-Inhibitors |
| Adolescent patient? | UVB |
| Methotrexate | In pustular or erythrodermic psoriasis consider: |
| Biologics | If MTX is ineffective or contraindicated consider: |
| | Fumaric acid |
A focus on pediatrics, comorbidities, infections, & biologics

Figure 2: Estimated PASI scores during 2-year follow-up in pediatric psoriasis patients with nail involvement (n=65) and without nail involvement (n=278) at baseline (Bronckers et al. 2019)

risk of developing more severe disease course. In a study of 343 pediatric patients with psoriasis, nail involvement was associated with more severe disease during 2-year follow-up (Figure 2). These findings suggest that nail psoriasis is a potential clinical predictor for more severe disease over time in these pediatric patients. It is important to search for more severe-disease predictors for in pediatric psoriasis because it would help clinicians improve individualized treatment.

REFERENCES

PATIENT CARE

IPC participates in survey of methotrexate dosing errors

In 2018, the European Medicines Agency (EMA), which oversees the safety and efficacy of medicines used in the European Union, invited IPC to participate in a review it was conducting of dosing errors associated with methotrexate medications. IPC Board Member Lluís Puig, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, responded to questions about methotrexate dosing in an EMA survey. In February 2019, IPC Councilor Catherine Smith, St Thomas’ Hospital, London, England, attended a meeting in London to discuss the issue. The EMA’s Pharmacovigilance Risk Assessment Committee (PRAC) reviewed feedback from IPC and other stakeholders, including oncology and rheumatology specialists, regarding patients inadvertently receiving daily instead of weekly doses of methotrexate-containing medicines. The committee’s review will identify potential reasons why such dosing errors occur and suggest risk measures to prevent them. The meeting highlights from this consultation review are now available on the EMA website. For more information on the PRAC review visit europa.eu/!mc88jK.

Latin America Working Group

This IPC working group, whose goal is to determine issues specific to Latin America, including access to care, education, and comorbidities, met during the recent RADLA (Annual Meeting of Latin American Dermatologists) congress in Buenos Aires, Argentina, to discuss planned projects and identify unmet educational needs in the region. They explored projects that included a survey of dermatology residency programs in Latin America and a literature review of psoriasis treatment options for patients affected by infectious diseases. Both projects aim to pinpoint gaps in knowledge regarding medical education and psoriasis management to ultimately raise the standard of care across the region. In addition, working group members received an overview of the recent IPC Master Class in Buenos Aires (see page 25) and they discussed opportunities to further engage program participants and to strengthen the content and planning of future programs in Latin America.

Biosimilars Working Group

IPC’s Biosimilars Working Group convened during the American Academy of Dermatology (AAD) Annual Meeting in March to finalize statements on biosimilar topics for a planned publication. The goals of the manuscript are to offer global guidance to clinicians, health care organizations, pharmaceutical companies, regulators, and patients regarding the development and use of biosimilars for treating psoriasis. Working group Co-chairs Arnon Cohen, Clalit Health Services, Tel Aviv, Israel, and Jay Wu, Dermatology Research and Education Foundation, Irvine, California, United States moderated the meeting. Dr. Cohen guided the group through a modified nominal group technique—a process that promotes group involvement in decision-making—that engaged the attendees in structured discussion. Statements were modified and finalized. Currently, the working group is conducting a biosimilar statement survey that will be included in the planned manuscript.

RESEARCH

Global Psoriasis Atlas: An update

Since it launched in September 2016, the Global Psoriasis Atlas has made remarkable strides in its long-term effort to create a comprehensive psoriasis database that will document the global burden of psoriasis. The GPA is a collaboration of the IPC and 2 other leading dermatological organizations, the International Federation of Psoriasis Associations (IFPA) and the International League of Dermatological Societies (ILDS). The group’s latest accomplishments were highlighted in its April newsletter. Among them:

• The atlas project has received a grant from the Global Challenges Research Fund (GCRF), which enabled a GPA team to present an educational workshop and to conduct a pilot survey of skin disease, emphasizing psoriasis, at the Regional Dermatology Training Centre in, Moshi, Tanzania, in July. The research fund, based in the United Kingdom, supports cutting-edge research in developing countries.

• GPA has established a Twitter account and will launch a new website on World Psoriasis Day, October 29.
• A GPA team has completed a systematic review of international data on the incidence and prevalence of psoriasis from population-based studies. The review will be submitted for publication to the journal Lancet Global Health.
• Another GPA team is evaluating access to health care for dermatology and health care in Latin America.

IPC Board Member Chris Griffiths, University of Manchester, Manchester, England, United Kingdom, is GPA director. Leading the GPA's working groups are IPC Councilors Darren Ashcroft, also of the University of Manchester, and Matthias Augustin, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. Find out more about the GPA at psoriasiscouncil.org/global-psoriasis-atlas.

Recently published IPC manuscripts

Abstracts and links to these articles are available at bit.ly/IPCpublications


Patient-reported outcome measures are important tools for capturing the patient experience and enhancing the patient-physician interaction. The Psoriasis Symptom Inventory (PSI) is a validated, 8-item instrument that assesses the severity of patient-reported psoriasis signs and symptoms. In 2017, IPC developed and executed a global study in partnership with Amgen that evaluated the practical usefulness of the PSI in clinical settings. The study's findings were published in an IPC-authored article in the June issue of the American Journal of Clinical Dermatology. The findings showed that completing the PSI questionnaire and subsequent discussion of the score with their physician encouraged patients to better communicate their experiences and treatment goals. Ultimately, the authors say, understanding patients' perspectives of their psoriasis symptoms will lead to patient-focused disease management. More information will be posted on the IPC website later this year regarding the availability of the PSI for clinical research and practice.


Corticosteroid therapy is regarded as first-line therapy for treating mild psoriasis and recalcitrant lesions. Members of the IPC Topical Therapies Working Group reviewed available international topical corticosteroids guidelines in order to understand current information and to identify areas that would benefit from greater practical guidance for dermatologists. The results of their review were published online by the Journal of Dermatological Treatment in May. The researchers reviewed corticosteroid guidelines from 10 countries: New Zealand, Norway, Malaysia, United Kingdom, the Netherlands, Scotland, Canada, the United States, Germany, and South Africa. In their article, the authors revealed that a broad consensus exists across guidelines regarding the choice of steroid potency for specific body sites and the duration of steroid use in the short term. However, the review demonstrated that there are gaps in the recommendations for long-term treatment, as well as in the utility of tapering of topical corticosteroids and breaks in treatment. The authors call for an international collaboration to develop a consensus opinion that would outline effective and safe real-world practice in the use of topical corticosteroids. Such a consensus would maximize the appropriate use of steroids for the benefit of patients with psoriasis.


IPC councilors, including Dr. Ruth Murphy, United Kingdom, participated in a consensus study that has developed clinical diagnostic criteria for plaque psoriasis in children and that has been published online by the British Journal of Dermatology. Dr. Murphy was senior author of the study, conducted by the Centre of Evidence Based Dermatology, University of Nottingham, United Kingdom, with the participation of IPC councilors interested in pediatric psoriasis. The article provides a list of expert-agreed diagnostic criteria developed through electronic eDelphi consensus methodology. In the article, the authors note that diagnosing psoriasis in children can be challenging and that no diagnostic criteria are currently available. They write that the consensus study is “the first step in developing diagnostic criteria” for pediatric psoriasis and that a diagnostic accuracy study is now...
underway to test them. The article's other authors, all colleagues of Dr. Murphy at Nottingham, are Dr. Esther Burden-Teh, Dr. Sonia Gran, and Professor Kim S. Thomas.


The use of biosimilars in 10 European countries to treat psoriasis is the subject of an IPC-produced article published online in the February 7, 2019, issue of *Current Dermatology Reports.* IPC Councilor Arnon D. Cohen of the Siaal Research Center for Family Medicine and Primary Care in Tel Aviv, Israel, is the lead author of the review, who collaborated with 14 IPC colleagues to produce the report. The article uses real-world information contributed by IPC councilors who are key opinion leaders in dermatology. Among its observations, the article notes that “some countries such as Norway, Denmark, and the United Kingdom have a relatively high market penetration of biosimilars, whereas in other European countries, biosimilar use is low.” Countries whose experiences with biosimilars described in the article include Austria, Denmark, France, Ireland, Italy, the Netherlands, Portugal, Spain, Switzerland and the United Kingdom. “The use of biosimilars for patients with psoriasis is continuously discussed and reviewed by the IPC through in-person meetings by members of (its) Biosimilars Working Group,” the authors write. The IPC, they say, will continue to lead efforts to adopt biosimilars into clinical practice and improve the choice of biologic treatment for patients with psoriasis.


Treatment goals for patients with psoriasis and worldwide barriers for optimal care are discussed in an IPC-produced article published in the March 9, 2019, issue of *Dermatology and Therapy.* The article summarizes a daylong IPC roundtable discussion that included key global opinion leaders whose topics included options for early treatment of all categories of psoriasis to alleviate the impact of the disease, and the need for policy changes that keep up with innovative therapies and that highlight greater understanding of treatment barriers in resource-poor countries. Lead author of the article is IPC Board Member Bruce Strober of the University of Connecticut Health Center, United States, who collaborated with 22 other councilors to produce the report.

**EDUCATION & OUTREACH**

**IPC symposium highlights ‘hot topics’ & challenging cases at AAD**

Councilor Arnon Cohen, Israel, was program chair for IPC’s Hot Topics satellite symposium presented in February at the 77th annual meeting of the American Academy of Dermatology (AAD) held in Washington, DC. Discussion sessions focused on managing psoriasis in women, treating palmoplantar psoriasis, international perspective in the use of biosimilar medications, and integrating biosimilars into clinical practice. Faculty for the sessions were IPC Councilors Robert Bissonnette, Canada, and Jashin Wu, United States, as well as dermatology professor Jenny Murase, University of California, San Francisco, United States. IPC’s report featuring summaries of psoriasis-related presentations made at the AAD meeting is available at bit.ly/AADHighlights.

**IPC presents Master Classes in Egypt and Argentina**

Earlier this year, IPC presented Psoriasis Master Classes in Cairo, Egypt, and Buenos Aires, Argentina. The Cairo course was IPC’s first Master Class to be offered in the Middle East. Launched by IPC in early 2018, the Psoriasis Master Class is a comprehensive educational program for dermatologists who want to expand their expertise in treating patients with psoriasis.

More than 60 dermatologists attended the 2-day Cairo class in April. Discussions addressed a variety of topics, including the pathogenesis of psoriasis, differential diagnosis, assessing psoriatic arthritis, psoriasis management, and challenging cases that were presented by both faculty and attendees. Serving as co-chairs were IPC Councilors Mahira El Sayed and Mohamed El-Komy, both of Cairo. Faculty for the class were Egyptian dermatologists Marwa Amer, Aya AlOrbani, Ahmed Nassar, Mahmoud Abdallah, and others.
Mona El-Kalioby and Mohamed Aideros, as well as IPC Board Member Chris Griffiths, United Kingdom, and IPC Chief Medical Officer Peter van de Kerkhof, the Netherlands.

In Buenos Aires, the Master Class was presented in early May prior to the Reunión Anual de Dermatólogos Latinoamericanos (Annual Meeting of Latin American Dermatologists), or RADLA. Discussions over the 2-day event covered a wide range of psoriasis-related topics, from an overview of the disease and clinical considerations (such as diagnosing psoriatic arthritis and assessing disease severity) to treatment options and management. The latter discussion addressed the major therapy options: topicals, phototherapy, systemics, biologics and biosimilars. Other sessions focused on scalp, nail, and genital psoriasis, as well as specific clinical scenarios such as pustular psoriasis, pregnancy, and pediatric psoriasis. Presentations of real-life, challenging cases rounded out the Master Class sessions, including one about the rare skin disorder pityriasis rubra pilaris and another about treatment-resistant psoriasis. Program chairs for the class were IPC Board Members Claudia de la Cruz, Chile, and Ricardo Romiti, Brazil. Councilors Matías Maskin, Argentina, and Fernando Valenzuela, Chile, served as regional faculty. International faculty were IPC Founding President Alan Menter, United States, and IPC Chief Medical Officer Peter van de Kerkhof, the Netherlands.

In 2018, IPC presented Master Classes in Mumbai, India, and Barcelona, Spain. At the time of this printing, IPC will have completed a Master Class in Chennai, India, representing the second time a program has been held in the country. Later this year, an additional program will be held in Vienna, Austria.

**IPC goes to RADLA**

Paradigms in the treatment of psoriasis, psoriasis in children, and noncicatricial alopecia were the topics discussed during a satellite symposium presented by IPC during RADLA (Annual Meeting of Latin American Dermatologists) held in Buenos Aires in early May. IPC Councilors Cristina Echeverría of Buenos Aires and César González of Bogotá, Colombia, were the program’s chairs. Dermatologists Enrique Rivas of Vista Hermosa, Guatemala, and Paula Luna of Buenos Aires served as faculty.
NEWSMAKERS

IPC Councilor Fernando Valenzuela, Santiago, Chile, has been elected to serve as president of RADLA 2024 (Annual Meeting of Latin American Dermatologists), which will be held in Santiago in 2024. Dr. Valenzuela will be in charge of organizing the conference, which will include scientific exchanges, teaching, and fellowship among Latin American dermatologists. RADLA scientific conferences are held yearly but planning for each one begins 5 years in advance, explains Dr. Valenzuela. Future conferences will be in Asunción, Paraguay (2020), Curitiba, Brazil (2021), Lima, Peru (2022) and Punta Del Este, Uruguay (2023). Dr. Valenzuela is associate dermatology professor at the University of Chile in Santiago. He is often featured as a main speaker at Latin American dermatology conferences.

At the recent Society of Investigative Dermatology (SID) annual meeting in Chicago, IPC Councilor Nicole Ward, United States, received a Research Achievement Award from the American Skin Association. Instituted in 1989 to identify established scientists in investigative dermatology and cutaneous biology, the award recognizes researchers who have greatly advanced work related to autoimmune and inflammatory skin diseases, melanoma and nonmelanoma skin cancer, as well as vitiligo and pigment cell disorders. Dr. Ward is an associate dermatology professor and director of the dermatology department’s Morphology Core of the Skin Diseases Research Center at Case Western Reserve University and University Hospitals Case Medical Center in Cleveland, Ohio. Her research primarily focuses on 3 unique but overlapping conceptual areas in psoriasis pathogenesis: skin inflammation drives remote vascular inflammation and thrombosis; neural activation of skin inflammation and proliferation; and elucidating a role for IL-17c and IL-17RE signaling in psoriasis pathogenesis. She was one of 5 researchers to receive the award.

CONGRATULATIONS TO IPC’S 2019 INTERNATIONAL FELLOWS

The IPC International Fellowship Program matches early-career dermatologists with IPC councilors and board members, providing an in-clinic shadowing opportunity up to 1 month, and a year-long mentorship. Chosen from a highly qualified international field of young dermatologists, our 2019 Fellows will be active participants in IPC programs with the world’s key opinion leaders, gaining exposure to clinical, research and educational skills that will further their careers as psoriasis leaders.

IPC’s International Fellows represent the future of psoriasis leadership and the organization’s commitment to grow expertise in the field.

Learn more at www.psoriasiscouncil.org/ipc_fellowship

Applications for 2020 Fellows will open on September 1, 2019

IPC would like to thank AbbVie and Janssen Biotech, Inc. for their support of the 2019 Fellowship program.
Psoriasis.
Our long-term commitment.

almirall.com
Alexander Navarini, MD, PhD
Basel, Switzerland

Professor Navarini is chairman of the dermatology department at the University Hospital of Basel. He was elected professor of immunodermatology, deputy head of the outpatient clinic, and head of the patch testing laboratory at the University of Zurich. Professor Navarini graduated from medical school at the University of Basel and Université Marie-Curie in Paris, France, in 2002. Between 2003 and 2006, he completed a postgraduate course in experimental medicine and biology and MD and PhD studies at the University of Zurich. His research focuses on next-generation genetics and gene hunting, as well as visual detection of skin diseases. He has published more than 130 peer-reviewed articles and several book chapters. He is currently principal investigator of the European Rare and Severe Psoriasis Network (ERASPEN) for harmonizing phenotype descriptions, as well as several clinical trials and the Swiss psoriasis registry.

George-Sorin Tiplica, MD
Bucharest, Romania

Professor Tiplica heads the 2nd Department of Dermatology at the Carol Davila University of Medicine and Pharmacy in Bucharest. He is involved in medical, research, and administrative activities. He served as research and development director of the Colentina Clinical Hospital in Bucharest and as executive director of the Romanian Society of Dermatology. His position as secretary general of the Romanian Medical Association linked him with the World Medical Association and the European Union of Medical Specialists (UEMS). He represents Romania on the European Academy of Dermatology and Venereology (EADV) board of directors and is a member of the EADV executive committee. His research interests include inflammatory skin diseases, wound healing, and sexually transmitted infections. He serves on the board of the International Union against Sexually Transmitted Infections (IUSTI-Europe).

Psoriasis took center stage at the annual AAD meeting, with presentations covering exciting preliminary results from ground-breaking studies that promise to revolutionize our understanding and treatment of this burdensome disease.

IPC’s report features summaries of significant psoriasis-related presentations made by distinguished international experts.

Find the report by writers Kevin T. Savage, BA, and Kelsey S. Flood, MD, online at bit.ly/AADHighlights
Changing the practice of medicine

At Novartis, we harness the innovation power of science to address some of society’s most challenging healthcare issues. Our researchers work to push the boundaries of science, broaden our understanding of diseases and develop novel products in areas of great unmet medical need. We are passionate about discovering new ways to extend and improve people’s lives.
THE INTERNATIONAL PSORIASIS COUNCIL IS PLEASED TO BRING YOU THE FOLLOWING EDUCATIONAL OPPORTUNITIES AND RESOURCES TO ADVANCE YOUR KNOWLEDGE OF TREATING PATIENTS WITH PSORIASIS.

UPCOMING IPC EVENTS

WEDNESDAY, SEPTEMBER 18, 2019
The mechanistic model(s) of psoriasis: Autoimmune and/or inflammatory?
49th European Society for Dermatological Research Meeting (ESDR)
Bordeaux, France

WEDNESDAY, OCTOBER 9, 2019
Hot topics and challenging cases in psoriasis: A focus on biosimilars, disease severity, drug survival, and systemic therapies
European Academy of Dermatology and Venereology (EADV) Congress
Madrid, Spain

FRIDAY, NOVEMBER 8, 2019
Dissecting psoriasis: Mechanistic studies in pustular and plaque psoriasis
44th Japanese Society for Investigative Dermatology (JSID) Congress
Aomori, Japan

IPC’S PROFESSIONAL EDUCATION & RESOURCE CENTER

ON-DEMAND WEBCASTS
Hot topics in psoriasis: A focus on pustular, biosimilars, pediatrics and treating in underserved areas
Filmed during an IPC Symposium at the World Congress of Dermatology in Milan, this series of on-demand webcasts addresses individualized treatment of psoriasis patients with real clinical practice approaches highlighting 4 important topics: pustular psoriasis, biosimilars, pediatric psoriasis, and treating in underserved areas. bit.ly/2019IPCwebcasts

TREATMENT GUIDELINES
A compilation of evidence-based guidelines for psoriasis diagnosis and management collected from around the world.

MEASUREMENT TOOLS
Commonly used measurement tools for psoriasis management and clinical trials.

ARTICLES & REPORTS
Psoriasis and atopic dermatitis: Similarities and differences
A joint publication of the International Eczema Council (IEC) and the International Psoriasis Council (IPC).

CONGRESS COVERAGE
Reviews of the psoriasis highlights from important congresses around the world.

PSORIASIS IMAGE LIBRARY
More than 500 images of different subtypes and phenotypes in psoriasis available for clinical and educational purposes.

VIDEO LECTURES
Search our library of challenging case presentations and lectures by topic and date.

Access IPC’s professional Education and Resource center at www.psoriasiscouncil.org/education
As more biosimilars become available around the world, it is important for dermatologists and others who provide care to patients with psoriasis to have a keen understanding of these treatment options and to be able to discuss biosimilars’ safety and efficacy with patients.

We are pleased to offer the following educational opportunities to health care practitioners around the globe:

**ON-DEMAND WebcamS:**

- Preparing for biosimilars
  Lars Iversen, Denmark

- Challenging case on biosimilars
  Lars Iversen, Denmark

  Presented at the World Congress of Dermatology (WCD), Milan, Italy

**Website Resources:**

View a comprehensive biosimilars reference library and make the best treatment decisions for your patients. Featuring on-demand webcasts, IPC published papers, and up-to-date information and tools from trusted sources.

psoriasiscouncil.org/biosimilars

**Upcoming Educational Symposium:**

- Hot topics and challenging cases in psoriasis: A focus on biosimilars, disease severity, drug survival, and systemic therapies

  28th Congress of the European Academy of Dermatology and Venereology (EADV), Madrid, Spain

  Wednesday, October 9, 2019
  9:00 am – 12:00 pm

  IFEMA Feria de Madrid
  North Convention Centre
  N109 – 110, Floor 1

This program is sponsored in part by Samsung Bioepis and Biogen.
Founded in 2004, the International Psoriasis Council (IPC) is a dermatology-led, voluntary, global, nonprofit organization with a network of more than 100 psoriasis experts, thought leaders, and professionals, dedicated to improving patient care around the globe.

Through our work, we deepen the understanding of the disease and its management. We lead advancements in care by facilitating cutting-edge research, convening partners to collaborate and advocate for improved treatment, and growing capacity for psoriasis management by sharing our knowledge. Unbiased and science-based, our collective expertise and influence have a direct impact on how patients around the world are treated.

OUR VISION IS A WORLD FREE OF PSORIASIS.

We believe that psoriasis patients, no matter where they live in the world, no matter how complex their symptoms, should have access to the best care available to them, and that ultimately a world without psoriasis is possible.

OUR MISSION IS TO IMPROVE THE CARE OF PEOPLE WITH PSORIASIS WORLDWIDE THROUGH EDUCATION, RESEARCH, AND ADVOCACY.

CO-EDITORS
IPC gratefully acknowledges co-editors Andrew Y. Finlay, MBBS, FRCP, dermatology professor, Cardiff University, Cardiff, United Kingdom, and Marcus Schmitt-Egenolf, MD, PhD, dermatology professor at Umeå University, Umeå, Sweden, for their writing and editing contributions to the July 2019 IPC Psoriasis Review newsletter.

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