Medicom International Conference Series in Dermatology

6th Congress of the SPIN

Skin Inflammation & Psoriasis International Network

25-27 APRIL 2019 • PARIS • FRANCE

PEER-REVIEWED CONFERENCE REPORT

What's New with Biologics
Recent advances in biologic therapies for psoriasis and eczema have changed patient outcomes, but how do we distinguish which patient responds better to which biologic treatment?

read more on PAGE 3

Managing Psoriatic Arthritis
Psoriatic arthritis-focussed outcome measures will steer the use of biologics. Treat-to-target using minimal disease activity as an objective will be the future of timely and effective psoriatic arthritis management.

read more on PAGE 6

Small Molecules
The value of small molecules will persist during the era of biologics. Tailored use, careful patient selection, and patient preference are all important determining factors when choosing a small molecule.

read more on PAGE 18

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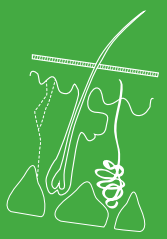
Contents



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ISSN 2468-8762 19:8

Letter from the Editor

Prof. Peter C.M. van de Kerkhof

Dear Reader,

The congress of the SPIN was a great opportunity to learn about innovations in the field of inflammatory dermatoses, in particular regarding psoriasis. Insights into the pathomechanisms and the mode of action of treatments have developed substantially during the last three years. Effective and safe control of psoriasis and eczema by targeted treatments has become reality.

Whereas topical therapies are the main stay in the first phases of psoriasis, systemic therapies become much more upfront, and dermatologists realise that psoriasis is, to a large extent, a systemic disease. It is the implementation of new biologics (three anti IL-17 molecules and three anti IL-23 molecules) together with the development of small molecules that revolutionises the treatment of psoriasis. On the same page, dermatologist realise the importance of early diagnosis of comorbidities of psoriasis.

The shift from short-term intervention to long-term, safe control was also reflected in the various presentations. Drug survival has become an important outcome measure. Further, biomarkers to predict treatment responsiveness of individual patients and to predict which patients are more likely to develop comorbidities are important research targets for the future.

This congress, at a crossroads from classical systemics and first-generation biologics to a future with innovative highly selective biologics and small molecules, was an outstanding opportunity to get a comprehensive insight into pathogenesis-based treatment of psoriasis. The congress gave a glimpse in the future of other inflammatory skin diseases with the promise of pathogenesis-based treatment for these diseases as well. The future for inflammatory skin diseases is bright.

Best Regards,
Prof. dr Peter C.M. van de Kerkhof
Senior professor of dermatology
Radboud University Nijmegen Medical Centre, the Netherlands

Biography

Peter C.M. van de Kerkhof is emeritus Professor of Dermatology and immediate past chairman of the Department of Dermatology of Radboud University Nijmegen. He is currently the coordinating Medical Officer of the International Psoriasis Council and chair of the scientific advisory board of the Dutch burn association. He has been working for many years on the pathogenesis and treatment of psoriasis. He has published more than 700 publications in peer-reviewed journals and has given many presentations on invitation at international conferences. He has served as president of the ESDR, EDF, and the International Psoriasis Council, and was board member of various international societies. Current interests are: pathogenesis and development of biomarkers for psoriasis; real clinical practise research; and personalised medicine.

Conflict of Interest Statement

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Aetiology: Triggers and Risk Factors

Understanding genetics to unravel psoriasis and atopic dermatitis pathogenesis

Recent advances in psoriasis and eczema genetics have not only led to innovative interventions and new drug pipelines, in some cases they also allow us to distinguish which patient responds better to which biologic treatment. Prof. Jonathan Barker (Kings College London, United Kingdom) discussed the direct clinical implications that psoriasis and atopic dermatitis (AD) genetics have realised [1]. Furthermore, the main genetic determinant for psoriasis, *HLA-C*06:02*, directs an autoimmune response against melanocytes through autoantigen presentation in psoriasis through ADAMTSL5, a melanocyte autoantigen [2].

Heritability is major factor of AD and psoriasis, as demonstrated in twin studies, where identical twins have a 25% concordance, whereas fraternal twins have only slightly higher concordance than the general population [1]. If a cohort has large numbers of adequately phenotyped patients, genome-wide association scanning (GWAS) can be an excellent technique to identify regions of genome that associate with disease. GWAS does not identify causative mutations, but it can provide evidence of association between a given locus and a disease manifestation, suggesting biological clues driving the disease of interest. For psoriasis, 16 loci have been identified by GWAS as being highly significant (see Table); 35 loci associate with AD.

Table: Overview of genetic determinants of psoriasis. Data from Barker (2019)

Affected function	Gene or locus
Proinflammatory pathways, innate immune activation, type-1 interferon activation, NF-kB cascade	Together these gene variants account for 20-30% psoriasis risk. Individual combinations of gene variants may modulate disease susceptibility, age of onset, or phenotype
T cell activation, differentiation, and signalling; IL-23/IL-17 axis	
Antigen processing and presentation	*PSORS1: HLA-C*06:02, HLA-C*07:01, HLA-C*07:02*, etc.; *ERAP1; PSMA6*

*HLA-C*06:02* (formerly called Cw6) is the major genetic determinant for psoriasis, granting an individual carrying this allele a 5-fold higher risk of developing psoriasis. The normal variant of this gene is important in presenting antigen to CD8 and natural killer T cells, which already speaks to the pathophysiology of psoriasis. About half of all psoriasis patients are *HLA-C*06:02* positive, as well as about 10-15% of the general population. The genetic effect of the *HLA-C*06:02* allele is greater than all other loci identified to date combined, at least for specific subtypes of psoriasis. For example, *HLA-C*06:02* is highly associated with early-onset and guttate psoriasis vulgaris, but not really with any other type such as late-onset psoriasis or psoriatic arthritis.

Filaggrin (encoded by the *FLG* gene) is the main genetic determinant of AD that came out of GWAS. The epidermal protein filaggrin is essential for regulation for epidermal homeostasis. Mutations lead to reductions in filaggrin expression. Mutations in *FLG* can also cause ichthyosis vulgaris. Depending on severity, 20-40% of patients with AD have *FLG* mutations. An individual with *FLG* mutation has a 3-fold higher risk of developing AD. However, >50% of individuals with mutation do not develop AD, in other words, *FLG* mutation is neither sufficient nor necessary to develop AD.

Neither *HLA-C*06:02* nor filaggrin are amenable to therapeutic intervention. However, GWAS provides evidence of other disease mechanisms. If you look at all of the hits from the large GWAS studies, many of the loci suggest genes regulating signalling pathways already implicated in psoriasis, like skin barrier function, interleukin (IL)-17 and IL-23 signalling, NF-kB signalling, and antigen presentation signalling. In the GWAS data from AD cohorts, the IL-13 pathway stands out, which we now know is so important. In brief, pathways that are amenable for intervention become evident when you overlay the genetics with the known immunology of the disease. For example, the dramatic clinical effect that tweaking IL-23 signalling has in psoriasis or tweaking the IL-13 pathway has in AD. The GWAS data from psoriasis and AD has genuinely contributed to the rich biologics available today, which has considerably improved patient outcomes.

Another approach is to look at functional exonic variants, and to ask whether they associate with a particular phenotype. Exome array is a technique that one can use to detect low frequency and rare coding single nucleotide polymorphisms.

When Prof. Barker and colleagues performed exonic arrays on over 11,000 psoriasis patients, only 2 genes strongly emerged. Multiple low frequency and rare protein coding variants in *IFIH1* (Burden 0.05, $1.8x10^{-19}$) and *TYK2* (Burden 0.05, $1.4x10^{-39}$) associate with psoriasis with exome-wide significance. *IFIH1* encodes the MDA5 protein, which plays an important role in innate immunity. In particular, the MDA5 protein targets viral double-stranded RNA, which may be a strong clue that there is an infectious agent involved in the pathogenesis of psoriasis. The second hit was TYK2, which encodes a member of the tyrosine kinase/Janus kinases(JAK) protein families. This protein associates with the cytoplasmic domain of type I and type II cytokine receptors and promulgates cytokine signals including IL-23 and interferon by phosphorylating receptor subunits. It is also a component of both the type I and type III interferon signalling pathways. Accumulating evidence suggest that *TYK2* plays a role in anti-viral immunity. A recent New England Journal of Medicine article shows impressive results in selectively inhibiting TYK2 in psoriasis patients with clear clinical benefit [3]. Prof. Barker stated: "This is a wonderful example of drug discovery being driven by genetics."

Genetics can also answer the question of causality. Psoriasis and obesity are well-known co-morbidities, but what has remained difficult is defining whether one causes the other or not. Mendelian randomisation is a genetic method to determine a causal relationship between phenotypes that minimalise confounding variables. When applied to obesity vs psoriasis, a study by Budu-Aggrey et al. concluded that obesity contributes to the pathogenesis of psoriasis [4]. Their results suggested that higher BMI causally increases the odds of psoriasis (by 9% for each unit increase in BMI). The study also concluded that no evidence suggested a causal effect of psoriasis on BMI. This type of genetic evidence supports a holistic approach to working with psoriasis patients, in a multidisciplinary team like many hospitals are developing now.

One last example Prof. Barker provided about the value of genetics was the recent understanding that *HLA-C*06:02* predicts response in psoriasis. Biologic-naive patients who were *HLA-C*06:02* positive and did not have psoriatic arthritis exhibited a significantly poorer (3x) response to adalimumab at 12 months [5]. A patient who has *HLA-C*06:02* should consider ustekinumab, but the opposite may not be true; there is no need to exclude patients with psoriasis from ustekinumab treatment because of a negative *HLA-C*06:02* genotype status. There are ongoing prospective studies to see if this can be validated into a clinically useful, genetics-driven, and practice-changing algorithm.

Prof. Jörg Prinz (Ludwig Maximilians University of Munich, Germany) picked up where Prof. Barker left off [2]. The main psoriasis risk allele, *HLA-C*06:02*, he explained, confers susceptibility to psoriasis by promoting melanocyte-specific autoimmunity through autoantigen presentation. Together with the identification of ADAMTSL5 as a melanocyte autoantigen, these results now allow for redefining the cascade of pathogenic events in psoriasis, defining an HLA class I-restricted autoimmune response against melanocytes as the central pathogenetic event. Thus, *HLA-C*06:02* confers an overall risk for psoriasis by facilitating an autoimmune response against melanocytes through autoantigen presentation, and gene variants related to innate immune activation and the IL-23/IL-17A axis may modify disease expression.

1. Barker J. O006, SPIN 2019, 25-27 April, Paris, France.
2. Prinz J. O019, SPIN 2019, 25-27 April, Paris, France.
3. Papp K et al. N Engl J Med. 2018 Oct 4;379(14):1313-1321. doi: 10.1056/NEJMoa1806382.
4. Budu-Aggrey A et al. PLoS Med. 2019 Jan 31;16(1):e1002739. doi: 10.1371/journal.pmed.1002739.
5. Dand N et al. J Allergy Clin Immunol. 2018 Dec 20. pii: S0091-6749(18)32780-5. doi: 10.1016/j.jaci.2018.11.038.

Atopic dermatitis and psoriasis: on a spectrum?

Prof. Emma Guttman-Yassky (Mount Sinai Medical School, USA) shakes down the similarities and differences between psoriasis vulgaris and chronic atopic dermatitis (AD) and concludes that they fall under the same pathomechanistic umbrella but with very distinct features [1].

For example, both psoriasis vulgaris and chronic AD are generally characterised by nearly indistinguishable histological psoriasiform dermatitis. At a mechanistic level we can classify both diseases as epidermal hyperplasia responses to certain cytokines produced by activated T cells in skin lesions, though the cytokines differ per disease [2]. About 12 years ago, a study comparing the expression of the proliferation marker Ki-67 by immunohistochemical staining of frozen sections of psoriasis and AD demonstrated that epidermal hyperplasia was equally evident in both psoriasis and AD [3]. This same study also found a similar extent of T cell infiltration in both the dermis and the epidermis in both diseases. However, the diseases exhibited very

"polar" immune responses when the cytokine profile was further defined; in psoriasis, IL-17, together with several Th17-associated products, was secreted by the activated T cells, whereas AD samples were characterised by Th2 cell responses like IL-13 production and other products of the Th2 pathway. The researchers of this study also detected an additional pathway being introduced by the Th22 cell, which they determined was important to the pathogenesis of AD but to a far lesser extent in psoriasis. In conclusion, it is generally believed that AD is Th2- and Th22-polarised while psoriasis is primarily Th17-driven, although there is some input from the Th22 pathway as well. Both diseases have characteristic contribution from the Th1 cell pathways, primarily in their chronic stage, but it is not known whether Th1 cells in this context are acting as bystanders or as a potential negative regulator of immune activation.

Some known differences and similarities between these diseases have been identified. In psoriasis, TNF- and iNOS producing dendritic cells (Tip-DCs) produce cytokines stimulating the 3 major players in psoriasis: Th17, Th22, and Th1 cells. IL-17 ligands activate IL-17 receptors on keratinocytes and immune cells and work in synergy with Th1 and Th22 cytokines to induce the clinical features of psoriasis. Cooperative actions of IL-17 and IL-22 lead to increased expression of the proinflammatory S100 proteins. IL-17 also directly or indirectly stimulates two cutaneous autoantigens (i.e. LL-37/cathelicidin and ADAMTSL5) that trigger a positive feedback loop driving further activation of Th17 cells. In AD, although the overall signalling and feed-forward loop is comparable, a different (inflammatory) dendritic cell initiates AD. Inflammatory dendritic cells are characterised by presence of the thymic stromal lymphopoietin (TSLP) receptor and OX40L ligand, and they in turn stimulate the three major types of T-cells mediating AD: the Th2-, Th22-, and Th1-cells. AD begins with an acute phase that is signified by excessive Th2-, Th22-, and Th17-cell activation. Transition to the chronic phase is marked by the onset of Th1-cell activation alongside the continued activation of Th2 and Th22 cells. TSLP, IL-4, and IL-13 may form a positive feedback loop whereby TSLP, produced by keratinocytes, drives Th2 polarisation. In part, this occurs through activation of dendritic cells, while IL-4 and IL-13 act on keratinocytes to further increase TSLP levels. Activation of Th2 cells leads to two AD hallmarks, including inhibition of barrier integrity proteins such as loricrin, filaggrin, and others, and reduction in lipids (i.e. free fatty acids and ceramides). IL-22 promotes hyperplasia, downregulates terminal differentiation, and synergises with IL-17 to induce the S100 genes, like in psoriasis. Prof. Guttman-Yassky pointed out that, recently, a molecular classifier has also added to the distinction between these diseases, with levels of CCL27 and iNOS being inversely associated in each disease (see Table) [4].

Table: Comparing psoriasis with atopic dermatitis: Same but different. Data from Guttman-Yassky (2019)

Psoriasis Vulgaris	Atopic Dermatitis
Adolescence/adult onset	Paediatric onset
Th17-dominant activity	Th2-dominant activity
Tip-DC infiltrate	IDEC/$F_c\varepsilon$R+ DC infiltrate
Very scaly/dry	Less scaly (spongiotic)/wet
Extensor surfaces	Flexor surfaces
Rarely infected	Infections common
Tendency for obesity	Not obese in most cases
Psoriatic arthritis is common co-morbidity	Asthma is common co-morbidity
IgE not elevated	High IgE in 80% of cases (Extrinsic)
No B cell involvement	B cell activation
Allergies are rare	Food and environmental allergies
Molecular classifier: ↓CCL27, ↑ iNOS	Molecular classifier: ↑CCL27, ↓ iNOS

Prof. Guttman-Yassky: "One concept that is new is that moderate-to-severe AD should be seen as a systematic disease, perhaps even more than psoriasis." Systematic inflammation is well established in psoriasis; however, little consideration of a systemic disease burden has been evaluated in AD. In a series of recent papers, researchers observed increased numbers of activated T cells in AD patients, not only when compared with healthy controls, but also when compared with patients with psoriasis. Increased immune activation has been recently reported in peripheral blood from AD vs psoriasis patients with evident increased circulatory cytokines in the periphery, again not only when compared with controls but even when compared with psoriasis patients [5-7].

1. Guttman-Yassky E. O010, SPIN 2019, 25-27 April, Paris, France.
2. Guttman-Yassky E, Krueger JG. Curr Opin Immunol. 2017 Oct;48:68-73. doi:10.1016/j.coi.2017.08.008.
3. Guttman-Yassky E, et al. J Allergy Clin Immunol. 2007 May;119(5):1210-7.
4. Garzorz-Stark N, et al. Exp Dermatol. 2016 Oct;25(10):767-74. doi: 10.1111/exd.13077.
5. Czarnowicki T, et al. J Allergy Clin Immunol. 2015 Jul;136(1):208-11. doi: 10.1016/j.jaci.2015.03.032.
6. Ungar et al. J Invest Dermatol. 2017 Mar;137(3):603-613. doi: 10.1016/j.jid.2016.09.037.
7. Brunner PM, et al. Sci Rep. 2017 Aug 18;7(1):8707. doi:10.1038/s41598-017-09207-z. Erratum in: Sci Rep. 2018 May 29;8(1):8439.

Advances in Therapy

Advances in target-oriented therapy: psoriatic arthritis

Prof. Wolf-Henning Boehncke (University of Geneva, Switzerland) provided an unorthodox presentation about psoriatic arthritis (PsA), highlighting aspects that are, as he put it, "to the left and right of what is in the current limelight" [1]. He argued that the lack of PsA-focussed outcome measures has possibly hindered the progress of innovative biologics in PsA patients as the gold standard of care, and he predicts that treat-to-target using minimal disease activity as an objective will be the future of timely and effective PsA management.

Steadily increasing recognition is being awarded to the fact that -like psoriasis of the skin- PsA can be multifaceted; however, unlike rheumatoid arthritis, PsA can affect tissues beyond the joints [2]. For example, Prof. Boehncke detailed, inflammation in PsA can result in swelling of an entire toe, especially associated tendons and their entheses (attachments to bone). There is an enormous benefit in coupling the knowledge from the rheumatology and dermatology fields in understanding and treating PsA. The pathogenesis of PsA shares many components of psoriasis pathogenesis known to dermatologists (e.g. tumour necrosis factor-alpha [TNF-alpha], IL-17, and IL-23), whereas rheumatologists have a few advantages when it comes to treating systemic disease with disease-modifying antirheumatic drugs.

In addition to the anti-IL-17 drugs used in psoriasis, rheumatologists treat PsA with non-steroidal anti-inflammatory drugs, which dermatologists of course would not use for the skin, as well as methotrexate and other drugs like leflunomide and sulfasalazine, they have access to 2 anti-TNF-alpha drugs which are not approved for psoriasis but only for psoriatic arthritis, as well as the PDE-4 inhibitor apremilast. The treatment decision landscape for PsA is complex and requires an algorithm taking 6 different domains into account to scope the current pharmacological therapies for PsA [3]. At the risk of oversimplifying this algorithm, Prof. Boehncke pointed out that TNF-alpha blockade seems to be the gold standard for treating PsA in the rheumatology world, yet so much new evidence has come out since the 2016 algorithm and the 2017 Ritchlin review in New England Journal of Medicine [2,3]. One important trend Prof. Boehncke explained is the use of minimal disease activity as a relevant endpoint for PsA, and this is a novel concept for dermatologists. The pivotal study was a 2018 trial of guselkumab -a selective IL-23 inhibitor targeting the p19 subunit- in PsA patients using minimal disease activity as the endpoint [4].

One exciting paper provided proof-of-concept about combined inhibition of IL-17A and IL-17F by bimekizumab [5]. The rationale for neutralising IL-17F together with IL-17A is that IL-17A and IL-17F are expressed at sites of inflammation and independently cooperate with other cytokines to mediate inflammation in humans. The clinical hypothesis is that neutralising IL-17F in addition to IL-17A will result in an improved complementary suppression of inflammation compared with inhibition of IL-17A alone. In addition to proving clinical efficacy of dual inhibition, the authors demonstrated on a molecular level that IL-17A works synergistically with IL-17F. They exposed synoviocytes to supernatants of Th17 cells and then tried to block the production of IL-17A, using recruitment of neutrophils as an in vitro readout. Then they did a deeper gene expression analysis, elegantly demonstrating that dual inhibition of IL-17A together with IL-17F normalised the expression of a number of genes that are relevant for joint inflammation. Prof. Boehncke said during his presentation: "This paper shows us that the IL-17 story is much more complicated that we previously thought […] it is not just IL-17A, it's F, it's E, it's C, and it's not just Th17 helper cells anymore, it's other cells as well." Inhibition of Janus kinase (JAK) for treatment of PsA has been discussed often this year; tofacitinib showed promising data at two doses, and performed as well as adalimumab vs placebo in psoriatic arthritis, demonstrating that tofacitinib is a fairly good drug for PsA [6]. Tofacitinib was also in the dermatology arena for a while, but the company has decided against pursuing tofacitinib for psoriasis, despite being approved, due to reported toxicities.

So, is TNF-alpha inhibition still the best treatment for PsA? The ECLIPSA trial challenges this dogma [7]. Prof. Boehncke

pointed out: "One bias becomes really evident when you reassess the trials performed [...] no one uses the psoriasis area severity index (PASI) score to measure atopic eczema, yet researchers use the ACR arthritis criteria to score PsA severity, for which there is absolutely no validation." Prof. Georg Schett (University of Erlangen-Nuremberg, Germany) and colleagues performed a single-centre retrospective study comparing ustekinumab with all the TNF-alpha inhibitors in PsA patients. The results, albeit not of the highest level of evidence, were astounding: while ustekinumab worked better on the skin as anticipated, no significant differences were observed with regard to tender and swollen tendons seen in psoriatic and rheumatic arthritis, but the data regarding enthesitis unequivocally demonstrated ustekinumab outperforming the TNF-alpha inhibitors. To understand this result, we should critically evaluate whether the ACR criteria perform well in PsA patients. Rheumatoid arthritis does not exhibit dactylitis, enthesitis, or nail involvement, and ACR does take these PsA-associated pathologies into account. Thus, one cannot use the old datasets demonstrating better outcomes for anti-TNF therapies because they always used ACR and therefore did not consider patient-relevant outcomes in patients with PsA. Developing a severity index and outcome measures appropriate and validated for PsA is essential, and once the data is disease-specific, it may well be that the anti-TNF dogma falls.

One well-known concept in many specialties including rheumatology, but still relatively unknown to dermatology, is the objective to treat-to-target (T2T). The primary outcome of the T2T concept is minimal disease activity. The definition of minimal disease activity in PsA trials has been repeatedly validated in numerous trials [8,9]: TJC ≤1; SJC ≤1; PASI ≤1; VAS pain ≤15mm; VAS Pat. Global Disease Activity ≤20 mm; HAZ ≤0.5; ≤1 painful enthesial site. The Coates group in Leeds (UK) put T2T to the test by asking whether using minimal disease activity as the treatment goal would improve hard patient outcomes like ACR and PASI. The TICOPA trial randomised patients into either standard care (office assessment every 2-3 months) or into a T2T arm where patients were assessed regularly every 4 weeks, and if the patient had not reached the treatment goal, the treatment was intensified. At the end of 1 year, all the outcomes including the ACR 20-50-70 and the PASI score were significantly better among the people in the T2T arm vs the standard of care arm [10]. The take-home message from this study is that using minimal disease activity is a flexible and aggressively worthwhile approach to control disease progression in early PsA patients.

A coordinated effort of Canadian rheumatologists and dermatologists looking at psoriatic disease generated a consensus statement concerning the application of the T2T concept for daily practice [11]. The summary of their T2T recommendations is as follows:

1 Clear or almost clear skin should be the target for psoriasis regardless of the area affected or duration of disease.
2 A state of minimal disease activity is a therapeutic target for psoriatic arthritis.
3 Quality of life is an important outcome and should always be a therapeutic target.
4 Functional impairment, comorbidities, and treatment risks should be considered in addition to assessing measure of disease activity.
5 Physicians and patients must agree on the selected therapeutic targets.
6 Patients must be treated adequately to reach the selected therapeutic targets, with therapy adjustments every 3 months for patients with active disease and every 6-12 months for static disease after therapeutic targets are reached.
7 The state of clear or almost clear skin should be maintained for as long as possible with adjustment in therapy at the first signs of disease progression.
8 Standard safety assessments should be performed at each visit.

In conclusion, numerous novel mediators of inflammation in PsA have been identified in the last few years and the field is changing rapidly. More importantly, some of these mediators have successfully been used as targets for innovative therapies, e.g. blocking IL-17F in addition to IL-17A, or the anti-IL-23 class of drugs. Assessment of individual PsA disease may be improved by replacing ACR criteria (which were not made with PsA in mind) with PsA-focussed measures, which may lead to the revision of current treatment algorithms and will likely challenging the dogma that TNF inhibitors are the superior drugs for PsA treatment. Dermatologists need to come to a joint decision-making era with rheumatologist in PsA treatment, and dermatologists need to share their experience with the innovative biologics, which are more effective than TNF-alpha blockade for psoriasis management. Rheumatologists may be hesitant to pursue these treatment options because ACR criteria are the only data collected so far. Lastly, T2T is about to become a widely established therapeutic strategy in other specialties and has been proven effective in PsA patients as well. Prof.

Boehncke concludes: "It is time for dermatologists to jump on this fast-moving train!"

1. Boehncke WH. O017, SPIN 2019, 25-27 April, Paris, France.
2. Ritchlin CT, Colbert RA, Gladman DD. N Engl J Med. 2017 Mar 9;376(10):957-970. doi: 10.1056/NEJMra1505557.
3. Coates LC, et al. Arthritis Rheumatol. 2016 May;68(5):1060-71. doi:10.1002/art.39573.
4. Deodhar A, et al. Lancet. 2018 Jun 2;391(10136):2213-2224. doi: 10.1016/S0140-6736(18)30952-8.
5. Glatt S, et al. Ann Rheum Dis. 2018 Apr;77(4):523-532. doi: 10.1136/annrheumdis-2017-212127.
6. Mease P, et al. N Engl J Med. 2017 Oct 19;377(16):1537-1550. doi: 10.1056/NEJMoa1615975.
7. Araujo et al. Semin Arthritis Rheum. 2019 Feb;48(4):632-637. doi: 10.1016/j.semarthrit.2018.05.011.
8. Coates LC, Helliwell PS. Arthritis Care Res (Hoboken). 2010 Jul;62(7):965-9. doi: 10.1002/acr.20155.
9. Coates LC, Helliwell PS. Rheumatology (Oxford). 2010 Sep;49(9):1793-4; author reply 1794. doi: 10.1093/rheumatology/keq138.
10. Coates LC, et al. Lancet. 2015 Dec 19;386(10012):2489-98. doi: 10.1016/S0140-6736(15)00347-5.
11. Gladman DD, et al. J Rheumatol. 2017 Apr;44(4):519-534. doi: 10.3899/jrheum.161473.

Favourable safety profile of long-term use of ixekizumab

Ixekizumab (IL-17A blocker) shows a consistent long-term safety profile in treating psoriasis with 5+ years of drug exposure in a large pooled database including 17,003 patient-years of exposure [1].

Results of this integrated analysis of 11 clinical trials were presented by Prof. Kristian Reich (Georg-August-University Göttingen, Germany), who pointed out that when it comes to drugs with which we only have limited experience, it is essential to capture data about safety as early as possible from as many patients as possible. A pooled analysis was performed of 11 controlled and uncontrolled phase 1-3 studies using ixekizumab in psoriasis totalling >17,000 patient years of exposure.

Prof. Reich: "The absolute numbers of safety events are actually very low here; infections are among the most frequent, but you have to treat 100 patients for 1 year to see 1 event, and this is in the ballpark with other targeted therapies." The incidence rate of serious adverse events, infections, major adverse cardiovascular events, malignancy, and depression did not increase with longer ixekizumab exposure. No unexpected safety outcomes were reported up to 5 years and the safety profile was consistent with previous reports in ixekizumab-treated patients. Allergic reactions or hypersensitivities were the most frequently reported adverse event. The authors concluded this data does not suggest that safety events are increasing over time, although they also warned that patients at very high risk may no longer take part in the in the study after long periods. Interestingly, the psychiatric comorbidity (i.e. depression/anxiety) of patients on ixekizumab appears to steadily reduce over time. To summarise, there is a good benefit-risk ratio for ixekizumab, class-specific safety, and target-specific safety. *Candida* infections were within the range of 2-3 events per 100 patient years, and there is no evidence that ixekizumab exacerbates inflammatory bowel disease.

1. Langley RG, et al. J Eur Acad Dermatol Venereol. 2019 Feb;33(2):333-339. doi: 10.1111/jdv.15242.

Brodalumab onset of action is significantly faster than ustekinumab: Results from the phase 3 AMAGINE-2 and -3 studies

Treating psoriasis patients with brodalumab achieves complete skin clearance more rapidly than ustekinumab. Although efficacy is obviously important, Dr Sandra Philipp (Charité-Universitätsmedizin Berlin, Germany) pointed out that patients rate the speed at which their disease improves as their most important treatment goal [1].

In the phase 3 AMAGINE-2 and AMAGINE-3 trials, Lebwohl et al. set out to describe and compare the onset of action, measured as the improvements in efficacy and quality of life, of brodalumab and ustekinumab in patients with moderate-to-severe psoriasis [2]. This pooled analysis included data from patients who were randomised to constant ustekinumab (n=590) or brodalumab (n=339) 210 mg every 2 weeks. Efficacy was measured at number of patients with 75% or 100% improvement in the psoriasis area severity index (PASI) score, the attainments of an absolute PASI score of 2 or less, and achievement of a Dermatology Life Quality Index of 0 or 1.

Patients treated with brodalumab had a far more rapid response and a significantly higher proportion achieved PASI-75 already at week 2 compared with ustekinumab (OR 8.5, P<0.001). Even more impressive was that patients treated with brodalumab had a >15 higher chance of achieving complete skin clearance (PASI-100) already after 4 weeks of treatment compared with ustekinumab (OR 15.6, P<0.001). This trend still holds true at week 12, at which point twice as many patients have achieved PASI-100. The take-home message was that both drugs may be clinically effective, but the greatest difference between the treatments is at the earlier timepoints; particularly for complete clearance at week 4. These results confirm the significantly faster onset of action

with brodalumab compared with ustekinumab in both clinical efficacy as well as patient-reported outcome measures.

1. Philipp S, et al. P006, SPIN 2019, 25-27 April, Paris, France.
2. Lebwohl MG, et al. N Engl J Med. 2015 Oct;373(14):1318-28.

Adalimumab vs adalimumab + methotrexate in psoriasis: First-year results on effectiveness, drug survival, safety, and immunogenicity

Dr Gayle van der Kraaij (Amsterdam UMC, the Netherlands) presented the first-year results from a Dutch/Belgian study that showed increased efficacy, adalimumab serum levels, and fewer antidrug antibodies when adalimumab is supplemented with methotrexate [1]. She explained the problem: adalimumab therapy is hampered by primary and secondary non-response. The lack of response is because in many patients only low serum drug levels can be detected, which is directly attributable to the formation of antidrug antibodies. The researchers sought to optimise adalimumab efficacy by applying a trick learned from rheumatoid arthritis, namely that the addition of methotrexate can alleviate this problem. The investigators performed a pragmatic randomised controlled trial in psoriasis patients, which was assessor-blinded in 5 hospitals in the Netherlands and Belgium. They compared adalimumab (n=30) vs adalimumab with methotrexate (10 mg/week supplemented with folic acid; n=31). All patients were eligible for adalimumab therapy according to the guidelines (PASI >8) and were adalimumab naïve. There will be follow-up every 12 weeks for 3 years, but because the trial is still ongoing, this presentation presented the key results for the first year.

Looking at the efficacy, significantly more patients in the combination arm reach PASI-75 at week 49 on adalimumab + methotrexate (58%) vs 31% in the monotherapy group (P=0.04). With regard to drug survival, patients on the combination arm have a slightly better drug survival at week 49, with 59% adalimumab vs 74% adalimumab + methotrexate; although these data are not statistically significant at this time point (P=0.26). Thirdly, the serum trough levels were significantly higher in the combination arm at about 6 mg/L (vs about 3.5 mg/L in patients treated with adalimumab alone). Lastly, antidrug antibody formation after a year was 47% in the adalimumab group vs 16% in the adalimumab + methotrexate (P=0.01).

1. Van der Kraaij G. P018, SPIN 2019, 25-27 April, Paris, France.

Ustekinumab for the treatment of moderate-to-severe plaque psoriasis in paediatric patients

Data from the CADMUS Jr study, presented by Dr Sandra Phillip (Charité-Universitätsmedizin Berlin, Germany), shows that ustekinumab is a highly effective and safe treatment option for children aged 6-12 years of age [1].

Psoriasis is a common disease and one-third of patients present in childhood. The objective of CADMUS Jr study was to evaluate the efficacy and safety of ustekinumab in paediatric (6-12 years) patients with moderate-to-severe plaque psoriasis. Therapeutic options are limited in those young patients. CADMUS Jr is a phase 3, open-label, single arm, multicentre (20 sites in 7 countries) study. The inclusion criteria were psoriasis area and severity index (PASI) score ≥12, a physician's global assessment score ≥3, percent body surface area affected by psoriasis ≥0%, and the patients had to be candidates for phototherapy/systemic treatment or considered by the investigator to be poorly controlled with topical therapy. Patients received a weight-based standard dose of ustekinumab administered by subcutaneous injection at weeks 0 and 4 followed by every 12-week dosing through week 40. The primary endpoint was a physician's global assessment of cleared (0) or minimal (1) at week 12, and major secondary endpoints were PASI-75 response at week 12 and PASI-90 response at week 12. Patients were considered non-responders after discontinuing treatment for lack of efficacy, an adverse event of worsening psoriasis, or use of a prohibited psoriasis treatment; zero improvement was assigned to these cases. After applying treatment failure rules, no other imputation tiles were applied except that patients with missing data at week 12 were considered non-responder. Safety was evaluated through week 56 (see Table). A total of 44 patients were included with a mean age of 8.9 years (range 6-11) and on average they had suffered from the disease 3.5 years on average with a mean PASI score of 17.9, indicating severe disease.

At week 12 the primary endpoint was reached; 77.3% achieved a physician's global assessment of cleared (0) or minimal (1) disease at week 12. A PASI-75 response was very good at week 12 in >80% of the patients and a PASI-90 in >60% of the patients. Importantly, this high response was maintained until week 52. The treatment was well tolerated. There were some adverse events mild-to-moderate infections, and only 12 patients had to be treated for them, and there was no patient that had to stop treatment due to adverse events.

Table: Overview of safety events through week 56. Data from Philipp (2019)

Average exposure (# administrations)	4.77
Patients who discontinued	0
Any adverse event	34 (77.3%)
Any serious adverse event: n (%)	3 (6.8%)
Overall infections: n (%)	29 (65.9%)
Infections requiring treatment: n (%)	12 (65.9%)
Serious infections: n (%)	1 (2.3%)
Malignancy	0
Anaphylactic reaction	0
Major cardiac event	0
Injection site reaction: n (%)	6 (13.6%)
Total number of injections	210
Injections with site reaction: n (%)	16 (7.6%)

1. Phillip S, et al. P025, SPIN 2019, 25-27 April, Paris, France.

Fumarates and vitamin A derivatives advance and latest insights in non-biologic systemic therapeutic agents in psoriasis and atopic dermatitis

Prof. Peter van de Kerkhof (Radboud University Medical Center, the Netherlands) presented situations where dimethyl fumarate might be considered as a first-line treatment for psoriasis. Acitretin (synthesised retinoic acid) has a potent activity in pustular psoriasis and erythrodermic psoriasis as monotherapy. In chronic plaque psoriasis, it has a strong therapeutic activity, particularly in combination with phototherapy/UVB. Dimethyl fumarate and acitretin have a unique profile; in patients with contraindications for immunosuppressive therapies, both therapies may provide a solution [1].

Dimethyl fumarate has a very long history, particularly in German-speaking countries and the Netherlands. EMA registration has now been filed, after which regulated pharmacovigilance will be enforced and active research will be extended to enhance the proper use of this drug. The European Guidelines on the systemic treatment of psoriasis vulgaris recommends fumaric acid esters for the induction and long-term treatment of psoriasis, applying a slow increased step-by-step dose regimen [2]. Prof. van de Kerkhof stressed that patient selection is key to decide whether a patient will benefit from dimethyl fumarate. It should be noted that dimethyl fumarate is not appropriate when you are going for the "quick fix", and that is not indicated for arthritis; so psoriatic arthritis patients should not be considered candidates for this alternative.

The advancement in the uses of drugs like dimethyl fumarate and acitretin comes down to the personalised treatment selection. For example, if you have a patient who requires systemic treatment because of unstable disease, consider the triggering factors of the patient. If there are underlying conditions that make a patient susceptible to infections, a systemic biologic treatment may not be the best choice. If there is no urgent need for rapid a resolution, and the patient is happy with a gradual improvement but wants a definite improvement without use of topicals, dimethyl fumarate may be an option. The patient may have chronic asthmatic bronchitis and needs antibiotics at times, so no immunosuppressive treatments would be indicated, or the patient may travel frequently to areas with endemic tuberculosis. Some patients should not receive strong immunosuppressive therapy.

However, if systemic therapy is indicated for such a patient, "my first choice would be dimethyl fumarate; the second choice would be acitretin (although there are some side effects), which has modest efficacy as monotherapy," said Prof. van de Kerkhof. Presuming that (1) a gradual improvement is requested/acceptable; (2) there is no arthritis; (3) in case of active infections, dimethyl fumarate can be continued; and (4) there are no concerns that the patient travels to areas with endemic tuberculosis. The dosage needs to be incrementally increased to avoid nausea. Once PASI-75 has been achieved, the dose could be incrementally and slowly reduced, and later increased again upon relapse. What is unique about this approach is the flexible dosing, which can be important for some patients.

Some notable side effects observed with dimethyl fumarate include gastrointestinal complaints, flushing, and lymphopenia. What is important to realise is that the efficacy increases with time and the maximal efficacy is observed after 12 months of treatment. This means that timely and appropriate management of toxicities is especially important for this therapeutic approach. In a series of patients receiving long-term care (max. 24 months), 41% patients developed lymphopenia and 12% had leucopenia. These conditions are important to recognise, but if the attending physician follows the clear lymphopenia protocol, assesses lymphocyte counts every 3 months, and intervenes when the counts get near <0.7 $x10^9$ cells/L, this side effect can be managed adequately.

One practical consideration regarding dimethyl fumarate is that the indication is not limited by a threshold PASI and can be first-line systemic therapy. It only mildly modulates the immune system and is therefore appropriate for cancer patients or can be used in patients at risk for infections. It can be used in combination with phototherapy or even in patients overtreated with phototherapy. If you follow the guidelines with respect to safety monitoring, this is an effective and safe treatment.

Vitamin A derivatives/retinoids do not have sufficient available evidence to generate an evidence-based recommendation for or against the use of acitretin as a monotherapy [3]. Based on clinical experience and depending on the opinion and the most important outcome for the individual patient, we suggest a low dose (10-30 mg daily) with respect to tolerability and a high dose (>30 mg daily) with respect to efficacy. For pustular psoriasis, the preferred dosage is 60 mg daily, and for erythrodermic psoriasis, the dosage is preferably 25 mg daily. Acitretin is not used often, but when biologics are not available, the combination therapy of acitretin and phototherapy may be an appropriate alternative for cases where systemic therapy is required, and an immunosuppressive therapy is contraindicated.

1. Van de Kerkhof P. SPIN 2019, 25-27 April, Paris, France.
2. Mrowietz U, et al. Br J Dermatol. 2017; 176(3): 615-623.
3. Nast A, et al. J Eur Acad Dermatol Venereol. 2015; 29(12): 2227-2294.

Certolizumab: Long-term safety and efficacy results for psoriasis-related nail disease

Pooled 48-week data from CIMPASI-1 and CIMPASI-2 phase 3 trials showed total nail disease resolution for approximately two-thirds (66.2%, n=133) of moderate-to-severe psoriasis patients with nail disease [1]. In addition, long-term safety data in psoriasis patients was presented. Lastly, dose escalation or continued treatment with 400 mg of certolizumab pegol every 2 weeks were shown to be effective treatment strategies for psoriasis patients who do not adequately respond to initial treatment.

The impact of certolizumab on nail disease in psoriasis patients was presented for the first time at SPIN 2019. Certolizumab pegol is a humanised antigen-binding fragment (Fab) of a monoclonal antibody that has been conjugated to polyethylene glycol. Certolizumab differs from other TNFα inhibitors in its lack of an Fc region, which minimises potential Fc-mediated effects such as complement-dependent cytotoxicity or antibody-dependent, cell-mediated cytotoxicity and is thought to be a factor in the prevention of active transfer of certolizumab pegol across the placenta during pregnancy [2].

Pooled 96-week safety data from the ongoing phase 3 certolizumab psoriasis trials, i.e. CIMPASI-1, CIMPASI-2, and CIMPACT, confirmed the long-term safety of certolizumab pegol in the treatment of psoriasis. In the 995 patients treated with at least one dose of certolizumab pegol for up to 96 weeks, no new safety signals were observed, and the safety profile was consistent with other anti-TNFs in psoriasis. The overall incidence of adverse events of interest was low; observed incidence rates of adverse events after 16 weeks were comparable for certolizumab pegol and placebo, and risk for adverse events did not appear to increase with longer exposure to certolizumab pegol up to 96 weeks (see Table).

Table: Overview of adverse events and serious adverse events to week 96 [1]

	All CZP (n=995)	CZP 200 mg Q2W (n=726)	CZP 400 mg Q2W (n=711)
Exposure (patient years)	1,471	772	700
Total AEs, IR (95% CI)	172.7 (161.1, 184.9)	161.4 (147.8, 176.0)	186.4 (170.9, 203.0)
Total SAEs, IR (95% CI)	9.2 (7.7, 10.9)	7.7 (5.9, 10.0)	10.8 (8.5, 13.7)
Most commonly reported AEs (≥10% patient, IR (95% CI)			
Nasopharyngitis	19.0 (16.6, 21.6)	19.4 (16.2, 23.1)	21.8 (18.3, 25.9)
Upper respiratory tract infection	10.3 (8.6, 12.2)	9.6 (7.4, 12.1)	11.9 (9.4, 14.9)
Selected AEs and SAEs of interest, IR (95% CI)			
Serious infections	1.7 (1.1, 2.5)	1.6 (0.8, 2.7)	1.7 (0.9, 3.0)
Active tuberculosis	0.1 (0.0, 0.4)	0	0.1 (0.0, 0.8)
Primary progressive multiple sclerosis	0.1 (0.0, 0.4)	0	0.1 (0.0, 0.8)
Congestive heart failure	0.1 (0.0, 0.4)	0	0.1 (0.0, 0.8)
Mailignancies (excluding non-melanoma skin cancer)	0.5 (0.2, 1.1)	0.7 (0.2, 1.5)	0.6 (0.2, 1.5)
Non-melanoma skin cancer	0.2 (0.0, 0.6)	0	0.4 (0.1, 1.3)
Discontinuations due to AEs, IR (95% CI)	4.3 (3.3, 5.5)	3.4 (2.2, 5.0)	5.5 (3.9, 7.5)
Severe AEs, IR (95% CI)	7.4 (6.0, 9.0)	6.6 (4.8, 8.7)	8.6 (6.5, 11.1)
AEs leading to death, IR (95% CI)	0.3 (0.1, 0.7)	0.3 (0.0, 0.9)	0.3 (0.0, 1.0)

AE, adverse event; CI, confidence interval; CZP, certolizumab pegol; IR, incidence rate; Q2W, every two weeks; SAE, serious adverse event; TNF, tumour necrosis.

Furthermore, findings from the phase 3 CIMPACT study demonstrated the efficacy of continued certolizumab pegol treatment for psoriasis patients who were partial responders (i.e. PASI≥50<75) or inadequately responded (i.e. did not achieve PASI-75) in the first 16 weeks of treatment. The results showed an important improvement in PASI-75, PASI-90, and PGA 0/1 response rates during an additional 32 weeks of treatment with 400 mg of certolizumab pegol every 2 weeks, both for patients who increased their dosing regimen from 200 mg of certolizumab pegol or those who remained on the dose regimen of 400 mg of certolizumab

pegol every 2 weeks. These data emphasise the importance of finding the right treatment regimen for individual psoriasis patients, and that certolizumab pegol is a potential effective long-term option for patients that inadequately responded in the first few months of their treatment.

1. Blauvelt A, et al. P032, SPIN 2019, 25-27 April, Paris, France.
2. Clowse MEB, et al. Arthritis Rheumatol. 2018 Sep;70(9):1399-1407.

Novel Considerations

Granulomatous rosacea: exploratory histological markers

In an initial histological profiling comparing granulomatous rosacea (GR) biopsies to erythematotelangiectatic rosacea (ETR) biopsies and to healthy controls, Dr EunHye Hong (Hallym University Sacred Heart Hospital, Korea) presented her data identifying that elevated numbers of mast cells and higher expression of toll-like receptor 2 (TLR2) are distinct to GR [1].

GR is a unique disease variant of rosacea, characterised by chronic relapsing inflammatory disease with various clinical features such as facial erythema, papules, flushing, pustules, and telangiectasias. Histopathologic findings feature characteristic non-caseated epithelioid granulomas. Little is known about the cell types involved in propagating GR or the underlying signalling that drives this disease. Neurovascular/neuroimmune dysregulation, which includes both anatomic and physiochemical differences present in rosacea-prone skin as compared with healthy facial skin, appears to be a major contributor that exacerbates the vasodilation of facial skin vasculature with increased facial blood flow that occurs during a rosacea flare [2].

Dr Hong and colleagues measured the differences in the expression rate of toll-like receptor 2 (TLR2), neurofilament, and mast cells in ETR (n=12), GR (n=12), and normal skin (n=11). All patients were diagnosed by clinical features and pathology-confirmed biopsies. The researchers performed quantitative analysis of immunohistochemical staining (i.e. number of pixels per image) and found no significant differences in neurofilament staining in any of the groups. GR had significant higher levels of mast cells than either ETR ($P<0.05$) or the control group ($P<0.001$); ETR was not significantly higher than the controls. For TLR2 expression, both ETR and GR had significantly higher levels than the control group ($P<0.05$ for both), although they did not significantly differ from each other.

Mast cells are key effectors in neurogenic inflammation and in rosacea evolution to a chronic stage. Since GR is a later-stage disease than other subtypes, Dr Hong speculated that mast cells may invade when the neurogenic inflammation begins to aggravate. In addition, research supports the observation that TLR2 triggers inflammation by kallikrein 5 (KLK5)-cathelicidin cascade. Increased TLR2 expression may be responsible for abnormal expression of KLK5 and cathelicidin, both of which are important in rosacea. Neurofilament is associated with neurogenic inflammation induced by neuromediators in sensory nerves, but no differences were noted between groups in this study, perhaps due to the sensitivity of the technique used.

The results of this study suggest that the increased expression of mast cell tryptase may be a sign of chronic later-stage GR. Increased expression of TLR2 suggests that cathelicidin-induced neuroimmune pathogenesis also contributes to the pathophysiology of GR. This was a small descriptive study, but it is suggestive that a larger scale immunohistochemical study is needed to confirm results on the pathophysiology of GR.

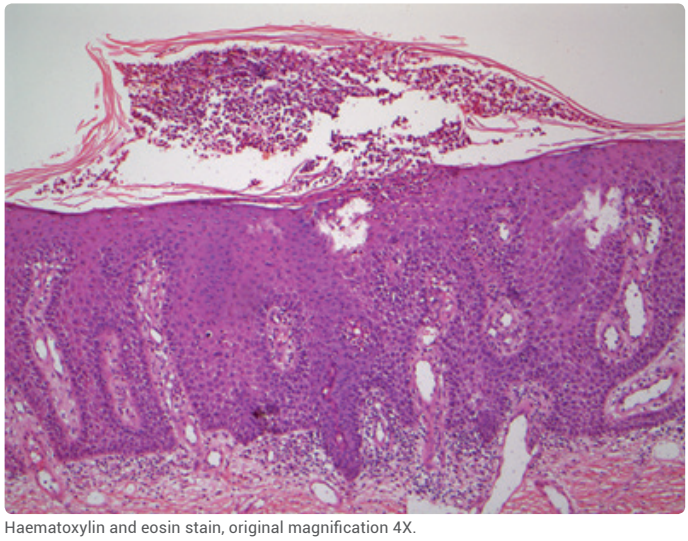
1. Hong E. P007, SPIN 2019, 25-27 April, Paris, France.
2. Two AM, Del Rosso JQ. J Clin Aesthet Dermatol. 2014 Jan;7(1):20-5.

Live imaging of cutaneous immune responses

Prof. Kenji Kabashima (Kyoto University, Japan) gave a visually stunning overview of the recent advances in intravital imaging techniques in mice, providing new avenues to study real-time molecular behaviour in intact tissues within a live organism [1].

The epidermis has >1,000 Langerhans cells per cm^2, and there are established mouse lines in which a fluorescent protein marks these cells. The monitoring of fluorescently labelled proteins and agents can be combined with autofluorescent properties of the microenvironment to provide a comprehensive snapshot of *in vivo* cell biology. Intravital or *in vivo* microscopy (IVM) has emerged as a powerful technique for the anatomical and functional mapping of cell biology in live mice from the subcellular level to whole-body approaches. The introduction of fluorescent proteins into mice by genetic engineering has opened exciting opportunities to track live cell biology and molecular dynamics *in vivo*. Combined IVM of fluorescent proteins with other fluorescently tagged probes, such as antibodies, drugs, or nanoparticles, while also exploring the inherent or autofluorescent properties of endogenous compounds, such as extracellular matrix or metabolites, can provide a comprehensive biological insight into live animals with an improved fidelity compared with cell and tissue-culture models. Furthermore, the use of multiphoton microscopy with pulsed infrared lasers provides key advantages for IVM as this can significantly extend the imaging depths owing to the reduced absorption and scattering at longer excitation wavelengths, while providing strong optical sectioning. Although Prof. Kabashima did not explore any single hypothesis in his talk, he demonstrated how his team uses models of ichthyosis vulgaris, among others, to video neutrophil activity and keratinocyte dynamics to gain exciting insights into the intricate regulation of live cell biology at the microscale level.

Figure: Psoriasiform dermatitis with a subcorneal pustule. Data on file



Haematoxylin and eosin stain, original magnification 4X.

1. Kabashima K. O020 SPIN 2019, 25-27 April, Paris, France.

Results from the ECLIPSE trial: does blocking IL-23 have better long-term outcomes in psoriasis?

Guselkumab demonstrated superior long-term responses compared with secukinumab in the treatment of moderate-to-severe plaque psoriasis in the first head-to-head trial (the ECLIPSE study) comparing an IL-23 inhibitor (guselkumab) to an IL-17 inhibitor (secukinumab); but there may be limitations to these data and more research is needed.

Prof. Kristian Reich (Georg-August-University Göttingen, Germany) reminded us that there are two main novel classes of drugs in psoriasis, the IL-17 and IL-23 inhibitors, and it will be interesting to discover what their similarities and differences might be in clinical outcomes [1]. The role that the cytokines play in the pathological cascade of psoriasis is very different; for example, while anti-IL-23 drugs can allow you to go to longer injection intervals, you have a very rapid onset of response if you block IL-17. What is also remarkable about this trial is that they use an unusual primary endpoint: the proportion of patients achieving a PASI-90 score at week 48. The reasoning behind this choice, Prof. Reich explained, was to get an idea about long-term disease control, which after all is more important to many patients than response at 4 weeks.

The objective of the double-blind ECLIPSE study was to compare efficacy and safety of guselkumab with secukinumab over 1 year of treatment for moderate-to-severe psoriasis, given that psoriasis is a chronic disease requiring long-term treatment. Patients were randomised to guselkumab 100 mg administered subcutaneously at weeks 0, 4, and 12; then every 8 weeks thereafter through week 44 (n=534); or secukinumab 300 mg subcutaneously at weeks 0, 1, 2, 3, and 4, and then every 4 weeks thereafter through week 44 (n=514). Primary and secondary endpoints were prespecified to be tested in a fixed sequence to control the overall Type 1 error rate. Patients were considered non-responders after discontinuing treatment for lack of efficacy, an adverse event, psoriasis worsening, use of a prohibited psoriasis treatment, if zero improvement was assigned, or if they had missing data.

The proportion of patients achieving PASI-90 response at all 7 visits from week 24-48 was 71.0% vs 61.5% in favour of guselkumab. Regarding safety, a higher *Candida* infection rate was observed in the IL-17 inhibition cohort -all easily

treatable with standard oral therapy- which was to be expected from clinical experience. And whereas there were 3 cases of inflammatory bowel disease in the secukinumab group, there were also several reported *de novo* melanomas in the guselkumab, but the numbers are still too low to really draw any conclusions. Overall, both drugs had good safety profiles in this study. The take-home message was that we need more head-to-head trials like this one to see where these drugs are similar, and where there may be distinct advantages of choosing one drug over another.

Table: Expert clinical opinion of Prof. Reich – A profile of targeted therapies in psoriasis [1]

	Anti-TNFs	UST	Anti-IL-17	Anti-IL-23
Plaques	++	++	+++	+++
Scalp	++	++	+++	+++
Nails	++	++	++	++
PPP	-	+?	+/-	+?
PsA Peripheral Spine Entestis/Dactylitis	 ++ ++ ++	 +/++ - ++	 ++ ++ ++	 +/++ - ++
Overall safety	+/ ++	++	+/ ++	++
Onset of response	+	+	++/ +++	++
Convenience/longevity	+/+	++/ ++	+ to ++/ ++	++/ +++

TNF, tumour necrosis factor; UST, ustekinumab; PPP, palmoplantar pustulosis; PsA, psoriatic arthritis.

1. Reich K, et al. P004, SPIN 2019, 25-27 April, Paris, France.

ABP501 biosimilar for adalimumab: What you need to know

Prof. Brian Kirby (St Vincent's Hospital, Dublin, Ireland) presented convincing data on the efficacy and safety of biosimilar ABP501 vs adalimumab in psoriasis patients [1].

Prof. Kirby began by reminding the audience that the development of targeted and effective biological therapies has transformed the outcomes for patients with psoriasis. Biosimilars are approved by regulatory authorities on the basis of rigorous clinical trials that demonstrate they are highly similar to the reference product in terms of quality, safety, and efficacy [2]. Minor differences in clinically inactive components must be supported by strong scientific evidence that these differences are not clinically meaningful. In general, they have lower acquisition costs than the reference product, and biosimilars have been shown to introduce price competition into the market, leading to reduced prices for the treatment of all patients [3]. Consequently, health authorities are increasing their use of biosimilars [4]. Each nation will develop policies on automatic substitution, automatic switching, and interchangeability. Reducing healthcare expenditure on biologics and releasing cost savings to support improved access to these important medicines by using biosimilars will play a vital role in ensuring that psoriasis patients can receive optimal treatment for their disease. The cost savings from biosimilars can improve patient access by broadening national reimbursement criteria to reach parity with European and other international guidelines. For both patients and healthcare providers, this may offer the benefit of improved clinical outcomes. At week 16, patients were blindly switched (or not). Patients were either on ABP501/ABP501 (n=152), adalimumab/adalimumab (n=79), or adalimumab/ABP501 (n=77), and were followed for a year. Switching made no difference (mean % PASI change was identical), showing identical efficacy and safety profiles but at significantly reduced costs.

1. Kirby B. FS02, SPIN 2019, 25-27 April, Paris, France.
2. Santos SB, Sousa Lobo JM, Silva AC. Drug Discov Today. 2019 Jan;24(1):293-299.
3. QuintilesIMS Report 2017. Retrieved from: https://ec.europa.eu/growth/content/impact-biosimilar-competition-price-volume-and-market-share-update-2017-0_en [Accessed 25 April 2019].
4. Moorkens E, et al. Front Pharmacol. 2016 Jun 29;7:193.

Switching infliximab biosimilars safe in treating chronic plaque psoriasis

Patients who switched between 2 different biosimilar infliximab products during treatment of chronic plaque psoriasis did not experience adverse events or change in severity [1]. In the study, 24 patients with psoriasis (12 of whom also had psoriatic arthritis) were switched from one infliximab biosimilar, CT-P13, to another, SB2. The patients, who had a previous exposure to CT-P13 of 23.2 (± 7.51) months, were then followed for 6 months after switching. Psoriasis Area and Severity Index (PASI) scores were measured at the time of the switch and at months 2, 4, and 6.

The investigators found that PASI scores at each measurement were substantially unchanged; mean scores at the time of the switch and at months 2, 4, and 6 were 0.67 (±1.38), 0.76 (±1.08), 0.71 (±0.93), and 0.42 (±0.62), respectively. In terms of adverse events (AEs), 2 infusion-related reactions, and 2 upper respiratory bacterial infections were observed in total. Despite the limited sample size and length of follow-up, the switch between the biosimilars, according to the researchers, was not associated with

a statistically significant change in PASI score or with increased AEs.

Switching among multiple products is increasingly common in countries where single-winner tenders for biosimilars are undertaken and in which patients may be asked to transition among products regularly based on the winner of the tender. However, few data is available concerning switches among multiple biosimilars of the same reference rather than between 1 biosimilar and its reference. Thus, the data from this present study marks a contribution to the literature and may provide reassurance to prescribers who have concerns about the safety and efficacy of switching among multiple biosimilars.

1. Gisondi P, Virga C, Girolomoni G. P049, SPIN 2019, 25-27 April, Paris, France.

Sustained and complete responses from the phase 3 AMAGINE-2 and -3 studies

A post-hoc analysis of the phase 3 AMAGINE-2 and AMAGINE-3 trials including 3,712 people with moderate-to-severe psoriasis showed that 90% of patients treated with brodalumab who achieved Psoriasis Area and Severity Index (PASI) score of 100 also experienced a sustained PASI-100 score [1].

In the same analysis, only 77% of patients treated with ustekinumab who achieved PASI-100 also experienced sustained PASI-100. The authors measured sustained PASI-100 as the time to inadequate response, based on a static physician's global assessment (sPGA) of ≥3 or persistent values of 2 over at least a 4-week period or after week 16. Since the subpopulations of patients treated with brodalumab and ustekinumab in these studies had different baseline characteristics, the authors did not apply statistical comparisons.

"Newer treatments for moderate-to-severe psoriasis have made it possible for patients to completely clear their skin, but the disease fluctuates over time; so we wanted to explore how fast and for how long patients can count on having complete skin clearance," said Prof. Lluís Puig (Hospital de la Santa Creu i Sant Pau, Spain). "These results show that brodalumab can offer more patients a longer, more sustained period of complete skin clearance than ustekinumab. That difference can have a big impact on patients' quality of life."

1. Warren, R. et al. P069, SPIN 2019, 25-27 April, Paris, France.

Reduction in coronary artery disease in psoriasis patients treated with biologic therapies, possible implications for atopic dermatitis

Treating psoriasis with biologic drugs that target the immune system can reduce early plaque build-up, which clogs arteries, restricts blood flow, and can lead to heart attacks and stroke. By extrapolation, this might also be beneficial to patients with chronic atopic dermatitis.

The association between psoriasis and occlusive cardiovascular events was noted originally nearly 50 years ago [1], and it is generally attributed to the heightened systematic inflammation present in psoriasis patients, which results in excess low-density lipoproteins lining the arteries. What was not yet known was whether modulating the inflammatory condition with immunotherapy would result in reduced risk of cardiovascular disease.

Dr Nehal Mehta (National Heart, Lung, and Blood Institute, NIH, USA) presented the just-published results of the first in-human evidence that treating psoriasis patients with biologic systemic therapies has positive consequences on cardiovascular outcomes [2]. This prospective, observational study of the NIH Psoriasis Atherosclerosis Cardiometabolic Initiative cohort included 290 psoriasis patients, 121 of whom suffered moderate-to-severe skin disease and qualified for the biologic therapy according to treatment guidelines. For a year, Dr Mehta and colleagues followed the entire cohort, all of whom had low cardiovascular risk at baseline, and compared the patients on biological treatments with those who did not receive biologic therapy. High-risk coronary plaque phenotypes were measured by coronary computed tomography angiography. A blinded reader (blinded to patient demographics, visit, and treatment) quantified total coronary plaque burden and plaque subcomponents (calcified and non-calcified) in the 3 main coronary vessels >2 mm.

Study results showed that biologic therapy was associated with an 8% reduction in coronary artery plaque, while other changes in other cardiovascular risk factors such as cholesterol, glucose, and blood pressure were unchanged. "The findings that intrigued us most were that coronary plaque sub-components changed over 1 year, including the necrotic core and non-calcified components, which are the culprits for most heart attacks," Dr Mehta said. These findings highlight that using biologic therapies to reduce the underlying inflammatory disease in patients has benefits in secondary complications, such as coronary artery

disease, in particular of rupture-prone plaque. However, it should be noted that this data is observational at this point, necessitating the initiation of randomised, controlled trials.

By extrapolation, biologic intervention might also be relevant for patients with chronic atopic dermatitis (AD), as pointed out by Prof. Emma Guttman-Yassky (Mount Sinai Medical School, USA). She noted that the AD transcriptome highlights atherosclerosis signalling in AD. The researchers took multiple profiles from AD patients and put them together in a meta-analysis approach, revealing the atherosclerosis pathway is one of the top pathways in AD patients [3]. Furthermore, many recent studies show an association between adult AD, cardiovascular disease, and increased heart attacks in 3 population-based studies [4]. In the NHANES study, flexural eczema in the past year was associated with significantly higher odds of cardiac arrest (P=0.04), heart attack (P<0.01), and congestive heart failure (P=0.02) but not with stroke (P=0.37) in survey-weighted multivariate logistic regression models that controlled for socio-demographics, comorbid asthma, and hay fever. The NHIS 2010 and 2012 studies reported that 1-year history of eczema correlates with a significantly higher odds of cardiac arrest (P=0.02), angina (P=0.02), heart attack (P=0.047), other heart disease (P<0.001), stroke (P=0.02), and PVD (P< 0.0001) in multivariate models. Collectively, this data is alarming, but the coming years will deliver clinical data with regard to the effects of timely control of systemic inflammation by innovative biologics.

1. McDonald CJ, Calabresi P. N Engl J Med. 1973 Apr 26;288(17):912.
2. Elnabawi YA, et al. Cardiovasc Res. 2019 Mar 15;115(4):721-728.
3. Ewald DA, et al et al. BMC Med Genomics. 2015 Oct 12;8:60.
4. Silverberg JI. Allergy.2015; 70(10): 1300-1308.

Treatment goals in psoriasis

Prof. Ulrich Mrowietz (University Medical Center Schleswig-Holstein, Germany) presented compelling data showing that addressing the risk (obesity and smoking) and trigger factors (infections like tonsillitis and periodontitis, stress) of psoriasis will be effective in disease modification and will reduce the number of psoriasis patients in the future [1].

In the concept of holistic management, there is one sphere of interlinked comorbidities interacting with the disease manifestation/phenotype (e.g. psoriasis and psoriatic arthritis). The care team must apply management procedures taking everything into account in order to decide the level of intervention and the sequence of this management. The most important first-level intervention is to pay attention to the risk and trigger factors. The second level of intervention would include the management of comorbidity. We need to be able to not only help the patient in weight-loss and smoking cessation, but also assist the patient with all aspects of their therapy. The third level of care in holistic management is to include everything to come up with a treatment plan that is most beneficial for that individual patient.

Obesity

Evidence suggests that managing risk factors such as obesity can be effective. Obesity is an independent risk factor for psoriasis, and a BMI>30 has shown to double the risk of psoriasis [2]. Furthermore, Prof. Elke de Jong (Radboud University Medical Center, the Netherlands) stated that obesity reduces treatment responses in psoriasis, as seen from real-world evidence from large registries [3]. The consequence of not paying attention to obesity and helping your patient to lose weight is that these patients will then be switched from one drug to another due to incomplete responses, entering a costly cycle that is ultimately detrimental to the patient as well. Obesity management is helpful in the treatment of psoriasis, as demonstrated by a 15-year-long Danish cohort study of obese people (BMI>30) who underwent gastric bypass surgery (1997-2012, n=12,364) compared with a similar number of Danish obese people who did not undergo surgery. The researchers looked at the risk of developing psoriasis in this cohort and showed that the risk of developing psoriasis was halved (HR 0.52) in patients who underwent gastric bypass surgery with the subsequent significant weight loss [4]. This data suggest that we could prevent half of all psoriasis cases if we are able to manage obesity in our populations; an impressive concept. A similar study in a Swedish population with a BMI>40, who were followed for 25 years, showed the same reduced risk if they underwent gastric bypass surgery [5]. For psoriasis, however, there is remarkably little data at this scale on the benefit of smoking cessation, and additional data on this topic is essential.

Tonsillitis

Managing trigger factors offers another layer of care for psoriasis patients. Tonsils/tonsillitis is an important trigger factor, particularly in children [6], and the mechanism of action of why tonsillitis triggers psoriasis is very well known. The T cells from the tonsils employ a cutaneous-associated

lymphocyte antigen as a homing factor, and their mistargeting of the skin can cause localised inflammation. Even years after tonsillitis, we can find the original tonsil-derived T cell clones back in the psoriatic plaques. The first data published on the beneficial effect of tonsillectomy in resolving psoriasis was a small Icelandic randomised controlled trial of 29 patients, in which patients were randomised to tonsillectomy or an observational arm without tonsillectomy [7]. The researchers reported that the treatment arm had immediate and sustained (>2 years) improvement of their psoriasis. Prof. Mrowietz is part of a team that reproduced and expanded this study and reported at this congress for the first time. Their aim was to identify which patient would derive the most benefit from prophylactic tonsillectomy. The Keil Tonsil Study prospectively tonsillectomised psoriasis patients (n=63) and monitored the change in their psoriasis severity scores following tonsillectomy. The data indicate that patients with <1 year since diagnosis of psoriasis have the greatest benefit over time. Patients who had had psoriasis for more than 1 year did not benefit very much from the surgery. Therefore, Prof. Mrowietz concludes that the earlier the patients are subjected to tonsillectomy, the better is the long-term outcome of the disease modification. In a subgroup analysis, comparing patient outcomes based on age, it was evident that the change in PASI scores was much larger in the younger, <18 years old, patients than in >18 adults. Thus, the recommendation of this study is to select patients for tonsillectomy early after onset of disease and as young as possible. The current paradigm is that only patients with tonsillitis will have their tonsils removed, but in this Keil cohort only a very few patients reported tonsillitis. In support, a subgroup analysis of a small, Swedish, retrospective study in patients with plaque psoriasis without a history of tonsillitis showed that 5 of the 8 patients who received a tonsillectomy experienced significant clinical improvement of their psoriasis, 3 remained unchanged, and none worsened [8]. In conclusion, apart from performing tonsillectomies in patients with tonsillitis, implementing tonsillectomy in the treatment of psoriasis in selected patients seems to be gathering evidence as a management option.

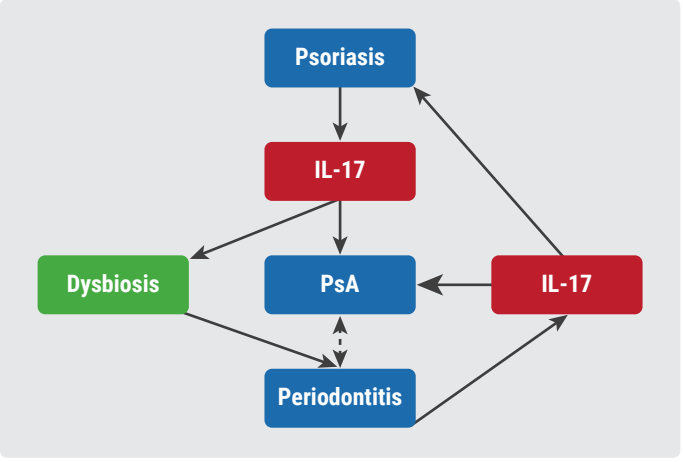
Periodontitis

Most dermatologists treating psoriasis patients will not typically look into the mouths of their patients, but the dental hygiene of psoriasis patients is critical and has tremendous implications. Most patients suffer from periodontitis, which is a disease that starts in the gingival crevice. It starts by changing the symbiont flora to a dysbiotic microbial community; thereby, stimulating an innate driven inflammatory response that also leads to bone resorption. One Danish study looked at 5.5 million Danes with mild/severe psoriasis or psoriatic arthritis and assessed their risk of periodontitis. This study convincingly demonstrated that with an increasing severity status of psoriasis, there is an increased risk of periodontitis (see Table). The risk is highest in patients with psoriatic arthritis. The underlying pathophysiology of periodontitis is highly analogous to psoriasis, as an IL-17-driven disease (see Figure). Levels of IL-17 in gingival crevice fluid is 5-10-fold higher in patients with periodontitis (n=49), compared to healthy controls (n=50) [9]. What is important to note here is that smoking is the most important risk factor for periodontitis, as well as being a risk factor for psoriasis. So, smoking cessation programmes are essential to support these patients to achieve disease modification.

Table: Summary of Danish population data of periodontitis risk association with psoriasis or psoriatic arthritis. Data from Mrowietz (2019)

	IR per 10,000 person years	Adjusted risk
Reference population (5.5 million)	3.07	--
Mild psoriasis (n=54,210)	5.89	1.66
Severe psoriasis (n=6,988)	8.27	2.44
Psoriatic arthritis (n=6,428)	11.12	3.48

Figure: IL-17 is central to psoriasis, psoriatic arthritis (PsA), and periodontitis [1]



Stress

An interesting investigation regarding stress compared newly recruited undeployed American soldiers (n=6,277) with those with post-traumatic stress disorder (PTSD)

after deployment in Afghanistan (n=5,583). The study then screened for risk-genes and associated diseases that are triggered by stress [10]. Surprisingly, only two diseases were more frequently found in the PTSD cohort: psoriasis (P=0.002) and rheumatoid arthritis (P<0.001). This data strongly suggests that there may be an underlying pleiotropy between PTSD and immunological disease, and that there might be a sub-cohort of psoriasis patients who are prone to stress disorders that later leads to disease aggravation. Much more data needs to be collected to understand the role stress plays as a trigger factor in psoriasis.

Addressing the risk factors (obesity and smoking), and the trigger factors (infections like tonsillitis and periodontitis in addition to stress) will be effective in disease modification where possible and will reduce the number of psoriasis patients. Researchers need to gather more data about the impact of smoking cessation, stress prevention, and dental health on plaque psoriasis.

1. Mrowietz U. O056, SPIN 2019, 25-27 April, Paris, France.
2. Wolk K, et al. Acta Derm Venereol 89: 492.
3. De Jong E. O058, SPIN 2019, 25-27 April, Paris, France.
4. Egeberg A, et al. JAMA Surg. 2017; 152(4): 344-349.
5. Maglio C, et al. Obesity 2017; 25(12):2 068-2073.
6. Prinz JC, et al. Clin Exp Dermatol 2001; 26: 326-332.
7. Thorleifsdottir RG, et al. J Immunol 2012; 188 (10): 5160-5165.
8. Nyfors A, et al. Dermatologica. 1975; 151: 216-222.
9. Apazidou DA, et al. J Clin Periodontol 2018; 45(10): 1173-1183.
10. Stein MB, et al. JAMA Psychiatry 2016; 73(7): 695-704.

Small molecules, apremilast, and TYK2

Prof. Richard Langley (Dalhousie University, Canada) contended that the value of small molecules will persist during the era of biologics [1]. Tailored use, careful patient selection, and patient preference are all important determining factors when choosing apremilast or TYK2 inhibition.

Many small molecules are being developed for psoriasis. They are small (<700 Da), chemically synthesised, generally simpler, well-defined, stable, and can be orally administered. Often, they are less expensive as well. Biologics, on the other hand, are generated in cell culture, are larger (>700 Da), and have complex tertiary structures with post-translational modifications; and the targets for biologics are usually extracellular (like anti-IL-17/-23) not intracellular (like small molecules). Currently, 3 (in some places 4) anti-TNF biologics are available: 1 anti-IL-12/23, 3 anti-IL-17s, and 4 anti-IL-23s, and many new molecules are coming out. In total, there are more than a dozen excellent options in first or second line. However, additional factors must be considered when choosing the right treatment.

For example, cost generally drives the use of methotrexate, but the reasons for choosing for apremilast are different. A recent study showed that the proportion of patients on apremilast report being extremely satisfied with their treatment vs biologics, especially with the ease of taking their treatment (P=0.018) and their comfort during treatment administration (P=0.002) [2]. There is also benefit for psoriatic arthritis patients, who are often on many medications like steroids and may not be candidates for biologics as a result, and it has a favourable safety profile.

Apremilast is an oral treatment with bioavailability of about 73%, with no food effect and a short half-life. It is a PDE4 inhibitor that is thought to have a dual effect repressing TNF-alpha, IL-23, and interferon-gamma while simultaneously increasing anti-inflammatory mediators like IL-10. The ESTEEM-1 and ESTEEM-2 studies showed the efficacy of apremilast at week 16 [3]. The CORONA psoriasis registry recapitulated similar responses for apremilast in real-world data.

In addition to being effective for psoriasis, apremilast has additional benefits. The pooled analysis of the phase 3 ESTEEM and PALACE trials and phase 3b LIBERATE trial demonstrated long-term haemoglobin (Hb) A1c changes in patients taking apremilast for psoriasis and/or psoriatic arthritis. The effect on Hb A1c could either be due to the reduction of inflammation or by induced metabolic changes; these data are entirely lacking but are of great interest if you have an overweight or borderline diabetic psoriasis patient [3]. The versatility of apremilast is further underscored by the effect apremilast has on oral ulcers after 12 weeks in patients with Behçet's syndrome [4].

Prof. Langley shared his expert opinion on the ideal candidate patient for apremilast: they would be a patient with moderate-to-severe psoriasis (with an emphasis on moderate) and stable disease who does not want to take a biologic, and, usually, other treatments have already failed to manage their disease. They may have comorbidities, as data from the CORONA database showed that patients with malignancies did well on apremilast, or can be on immunosuppressants already.

Prof. Langley ended with a few slides about TYK2 inhibition. TYK2 is interesting because it mediates signalling of fewer

cytokines than its fellow Janus kinases, and is considered highly selective. BMS-986165 is a molecule that binds to a regulatory domain of TYK2 and changes the conformation such that the kinase activity is inactivated. The rationale is that it is highly selective in blocking IL-23, IL-12, and type 1 interferon signalling but does not block the binding site, and so it does not impact other Janus kinases, resulting in fewer off-target effects. The initial efficacy rates look very good and the safety profile is good, but convincing phase 3 data will be necessary to demonstrate its true narrow selective effects.

In conclusion, small molecules are usually desired by the patient. The benefit-to-risk ratio is good although the benefit aspects should improve with incremental improvements. Small molecules are attractive for paediatric patients as well as adult patients with complex comorbidities.

1. Langley R. 0039, SPIN 2019, 25-27 April, Paris, France.
2. Lee LK, et al, AAD 2019 Poster 8254.
3. Puig L, et al. JAAD 2018; 79(3): Suppl. 1, AB151.
4. Hatemi G, et al. N Engl J Med. 2015 Apr 16;372(16):1510-8.

Prof. Jo Lambert

President of the SPIN
Ghent University, Belgium

Medicom asks Prof. Jo Lambert (President of the SPIN):

Can you tell us what sets SPIN apart as an organisation?

Prof. Lambert: SPIN's mission is to improve the quality of healthcare for patients suffering from chronic inflammatory diseases, in particular for psoriasis and atopic dermatitis. SPIN elaborates its mission through working with a carefully built national and international network, of patients and healthcare providers, with whom we are very closely in contact. They offer us valuable information on the needs and concerns in the field, which we then lift to a higher level. We are different from other organisations in the sense that we are very much a 'bottom up' organisation. Of course, our 3-yearly congress is a major highlight in our activities, but next to that we offer practical tools to enhance your practice on our website, and we focus on educational modules, trying to expand knowledge in areas such as 'how to set up a good clinical trial?', 'medical writing', and other aspects of professional engagement.