



Personalising Psoriasis Care: From Genetic Drivers to Dietary Interventions

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PSORIASIS is no longer regarded as a single, uniform condition. Once classified primarily by visible lesions or severity, it is increasingly understood as a spectrum of inflammatory disorders with distinct molecular drivers, genetic signatures, and clinical trajectories. In a session titled 'Psoriasis', this year's European Academy of Dermatology and Venereology (EADV) Congress brought together leading experts to explore how insights on endotyping, early aggressive treatment, oral therapies, and dietary interventions are reshaping patient care.

REDEFINING PSORIASIS THROUGH ENDOTYPES

Denis Jullien, Professor of Dermatology and Head of the Department of Dermatology, Hôpital Edouard Herriot, Hospices Civils de Lyon, University of Lyon, France, began the session by introducing endotypes, a framework for reclassifying psoriasis based on its molecular and immunological underpinnings rather than traditional phenotypes. "What the concept of endotypes tries to do is rationalise psoriasis diversity by stratifying the disease into subgroups that share molecular (and that's the main word here) characteristics," he explained. While dermatologists have long categorised patients by clinical features, Jullien emphasised that these classifications fail to capture the biological diversity underpinning disease behaviour.¹

Endotyping seeks to identify subgroups of patients who share common mechanisms, genetic variants, or immunologic pathways, offering the potential to predict disease course, tailor treatment, and understand differential therapeutic responses.¹ He highlighted IL-36-driven pustular psoriasis and emerging monogenic forms linked to *ADAR1* mutations as examples of

molecularly distinct subtypes with clinical significance.^{2,3}

Continuing, he explained that large-scale genomic, transcriptomic, and cellular studies are transforming our understanding, linking susceptibility variants to treatment response and classifying skin lesions into molecular subtypes. Biomarkers such as monocyte phenotypes and spatial transcriptomics could soon allow clinicians to differentiate mild from severe disease, moving beyond surface-level observation toward precision medicine.

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"The clinical translation of endotype knowledge holds immense promise for precision medicine in psoriasis," Jullien concluded, highlighting that a move from phenotype-driven to mechanism-driven classification could revolutionise treatment selection and long-term outcomes.

HIT EARLY, HIT HARD

Building on the concept of tailored care, Andrew Blauvelt, Blauvelt Consulting LLC, Lake Oswego, Oregon, USA, explored whether the timing and intensity of treatment could reshape disease trajectories. He proposed a provocative strategy: 'hit early, hit hard'.⁴ Rather than focusing on incremental symptom control, Blauvelt argued that early, aggressive therapy could deplete pathogenic immune cells and extend remission, potentially altering the natural history of psoriasis.

Evidence increasingly supports this approach. Patients with short disease duration respond more robustly and maintain remission longer than those with long-standing disease. Studies such as STEP-IN (secukinumab)⁴ and GUIDE (guselkumab)⁵ showed higher clearance rates and delayed relapse in early-treated patients. Mechanistic studies revealed that resident memory T cells, key drivers of recurrent disease, are more effectively depleted in early-treated patients, providing a biological explanation for prolonged remission.⁶

Blauvelt also examined 'hit hard' strategies, including the KNOCKOUT study,⁷ which

tested high-dose risankizumab at up to four-times the standard dose. The findings showed that 83% of participants achieved Psoriasis Area and Severity Index (PASI) 100 at Week 28, and a subset remained disease-free for 2 years without additional safety concerns.⁷ Looking forward, he explained that next-generation IL-23 inhibitors are being designed to optimise pharmacokinetics for prolonged efficacy, testing the combined 'hit early, hit hard' concept in clinical practice.

He concluded with cautious optimism that early, intensive intervention may bring clinicians closer than ever to durable remission, challenging the notion that psoriasis is inevitably chronic and progressive.

ORAL THERAPIES: EXPANDING ACCESS AND OPTIONS

Richard Warren, Professor of Dermatology, The University of Manchester, UK, shifted the focus to oral systemic therapies, exploring their evolving role in an era dominated by biologics. While injectable biologics achieve high efficacy, oral agents remain essential for many patients due to convenience, needle aversion, logistical



challenges with home-administered treatments, and accessibility issues in global healthcare settings.

Warren reviewed two key therapeutic classes. Phosphodiesterase-4 (PDE4) inhibitors offer a well-tolerated option without laboratory monitoring, though efficacy remains modest.^{8,9} Next-generation PDE4 agents have shown promising Phase II efficacy, particularly in achieving PASI 90 responses, but require Phase III validation.^{10,11} Warren explained that tyrosine kinase 2 inhibitors have been shown to have improved efficacy compared to PDE4 inhibitors, while maintaining a well-tolerated safety profile and stable long-term responses. Emerging agents also show the potential to bridge the gap with biologic therapies, offering higher PASI responses and retention of effect.^{8,12,13}

DIET AND LIFESTYLE: COMPLEMENTARY STRATEGIES

The final speaker, Wendy Hall, Department of Nutritional Sciences, School of Life Course & Population Sciences, King's College London, UK, provided an insightful perspective by examining the role of nutrition in psoriasis management. She explained that patients often ask whether dietary modification can improve symptoms, but robust evidence has historically been limited.

She emphasised the necessity to consider the impact of diet on disease burden in psoriasis. Excess adiposity worsens disease severity and reduces biologic responsiveness, diet influences cardiometabolic comorbidities, and sleep and mental health challenges can affect eating behaviours.¹⁵

Reviewing existing guidelines, Hall noted that advice primarily focuses on weight reduction, yet one-third of patients with psoriasis have a BMI under 25, highlighting the need for interventions beyond simple weight control.¹⁶ She also explained that observational studies suggest that higher adherence to a Mediterranean diet, dietary approaches to stop hypertension, or plant-based diets correlates with lower psoriasis severity, whereas red and processed meat, sugar, and salt intake is linked to worse outcomes.

Hall then shared results from the METRED-P pilot study,¹⁷ which tested Mediterranean and time-restricted eating approaches. Both interventions were feasible, improved quality of life, and reduced self-assessed psoriasis severity. Mediterranean diets enhanced well-being, while time-restricted eating produced modest weight loss, demonstrating that different dietary strategies may confer complementary benefits.

She emphasised the importance of individualised approaches and dietitian support, highlighting that while diet “does matter,” larger, well-powered trials are required to establish causality and refine recommendations.

“**Early, aggressive therapy could deplete pathogenic immune cells and extend remission, potentially altering the natural history of psoriasis**”

Perhaps most striking, Warren highlighted oral peptides, including a novel, investigational IL-23 receptor antagonist developed using AI to target cytokine binding pockets. Phase III trials have demonstrated near-biologic efficacy, with particularly promising results in high-impact areas such as the scalp and genitals.¹⁴

These innovations mark a paradigm shift, combining oral convenience with biologic-level efficacy, expanding the reach of systemic therapy, and allowing patients with high disease burden but limited body surface involvement to access meaningful treatment. Warren concluded that oral therapies will play an increasingly central role in precision, patient-centred psoriasis care.

INTEGRATING ADVANCES INTO CLINICAL PRACTICE

Across sessions, a common theme emerged: psoriasis care must integrate molecular insights, treatment timing, therapeutic modality, and lifestyle factors. Endotyping offers the potential to classify patients according to biological mechanisms, guiding therapy selection and predicting outcomes. Early, intensive

treatment may alter disease trajectory, while oral therapies expand access and convenience without compromising efficacy. Nutrition and lifestyle interventions offer complementary support, particularly in mitigating comorbidities and enhancing well-being. Together, these approaches support a move toward precision, personalised, and patient-centred care.

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