EADV 2024

The purpose of the EADV is to foster knowledge exchange, improve the quality of dermatology care, and inspire advancements in dermatology research

Congress Review

Review of the European Academy of Dermatology and Venereology (EADV) Congress 2024

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THIS YEAR saw the 33rd European Academy of Dermatology and Venereology (EADV) Congress that, for the third time in its history, was hosted in Amsterdam, the Netherlands. With over 160 symposia, 20 subspeciality sessions, and the ever-popular 'Late breaking news' sessions, EADV President Martin Röcken described this as the biggest year so far, with more than 17,000 participants involved in the event. Being a hybrid event, EADV committed to live-streaming all sessions, making content available on-demand to improve the reach of the Congress and maximise the inclusivity of the event.

Concluding his introduction, Röcken touched on how the focus for the EADV Congress 2024 centred around building a "bridge to the future", a nod to the 1,200 bridges that make an elaborate web throughout the city of Amsterdam.

Dirk Jan Hijnen, Erasmus University MC, Rotterdam, the Netherlands, warmly welcomed all those at the opening ceremony to the city, jovially remarking that those attending in person should beware when out on the street, scanning for the 1.33 bikes there are per person in Amsterdam. Turning to the new programme additions, Hijnen highlighted the Residents' Track, which was designed to engage young dermatologists at the early stages of their careers. He remarked that the purpose of the EADV is to foster knowledge exchange, improve the quality of dermatology care, and inspire advancements in dermatology research across Europe, by offering an excellent opportunity for attendees to start new collaborations, exchange ideas, and build meaningful connections within the dermatology community.

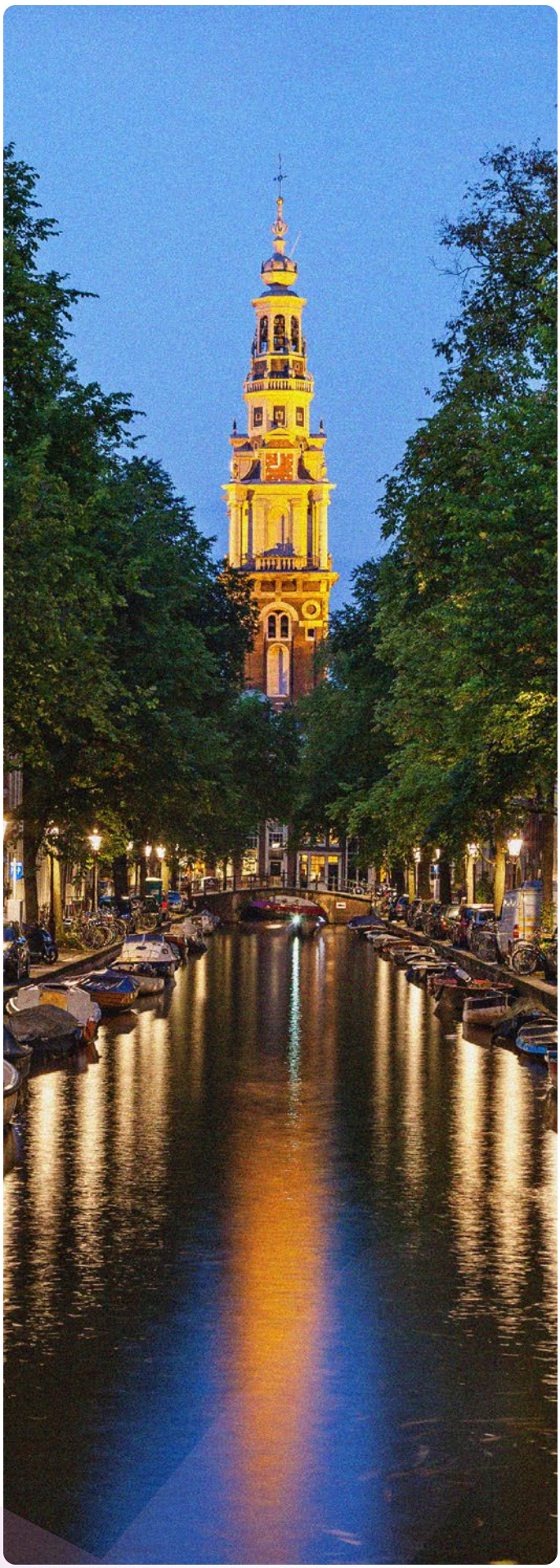
The rest of the opening ceremony focussed on looking to the future as the keynote lecture, presented by explorer and psychiatrist Bertrand Piccard, Lausanne, Switzerland, discussed renewable energy and clean technologies which, as Piccard described, are the new medications for our world. Piccard described how the 20th century brought significant progress in life expectancy, public health, and quality of life, yet, as we venture further into the 21st century, we face daunting challenges that seem to unravel these achievements. Unsustainability, pollution, depletion of natural resources, and the extinction of biodiversity signal a dangerous regression. He stated: "Our mission must be to heal the planet," not just individual patients, and fortunately, we have the "medication" for this

cure: renewable energy, energy efficiency, and sustainable practices. He noted that implementing these solutions requires radical change, and achieving compliance with this regime on a global scale is far more difficult than gaining compliance from a single patient. However, Piccard assured the audience the belief that these changes are impossible exists only in the mindset of those who assume the future will simply be an extrapolation of the past, and the truth is that the future is open to change and subject to disruption. The keynote lecture ended with the inspiring note that history is filled with paradigm shifts, from the moon landing to the ascent of Everest, and these feats were achieved by people who broke the rules and redefined limits. The audience members were encouraged to embrace the notion that innovation happens not when a new idea emerges, but when an old belief is cast aside.

> **Our mission must be to heal the planet**

Key topics from the event included the cardiovascular effects of JAK inhibitors in atopic dermatitis, personalised biomarker approaches to treatment, CAR-T therapy for refractory systemic lupus erythematosus, and the treatment of vitiligo and moderate-to-severe atopic hand eczema.

EMJ had the pleasure of attending the EADV Congress 2024, and is excited to share highlights from the late-breaking news sessions. Continue reading for an in-depth look at the latest research updates from this year's Congress as we look forward to being part of the EADV community at next year's meeting in Paris, France.



JAK Inhibitors Show No Cardiac Risk in Atopic Dermatitis Treatment

JAK INHIBITORS have become essential treatments for moderate-to-severe atopic dermatitis (AD), a condition affecting up to 20% of adolescents and 10% of adults worldwide. Despite their proven effectiveness, some dermatologists remain cautious when prescribing these medications due to concerns about their potential association with major adverse cardiac events (MACE).

This retrospective cohort study, presented at the EADV Congress 2024, aimed to assess the incidence of MACE and other cardiovascular conditions in patients with AD treated with upadacitinib or abrocitinib. Although JAK inhibitors have been linked to cardiovascular issues in treating other inflammatory skin conditions, there is limited data on their safety, specifically in patients with AD. Understanding these risks is critical for dermatologists when considering treatment options for patients who have not responded to conventional therapies.

The study utilised data from the TriNetX Research Network, identifying patients diagnosed with AD, and selecting a cohort consisting of 1,802 patients treated with upadacitinib or abrocitinib. The control cohort included over 1.2 million patients with AD who had never been treated with these medications. However, to ensure a balanced comparison, both cohorts were propensity-score matched based on factors such as age, biological sex, and cardiovascular comorbidities, resulting in 1,802 patients in each group. The incidence of cardiovascular events was then analysed in both groups.

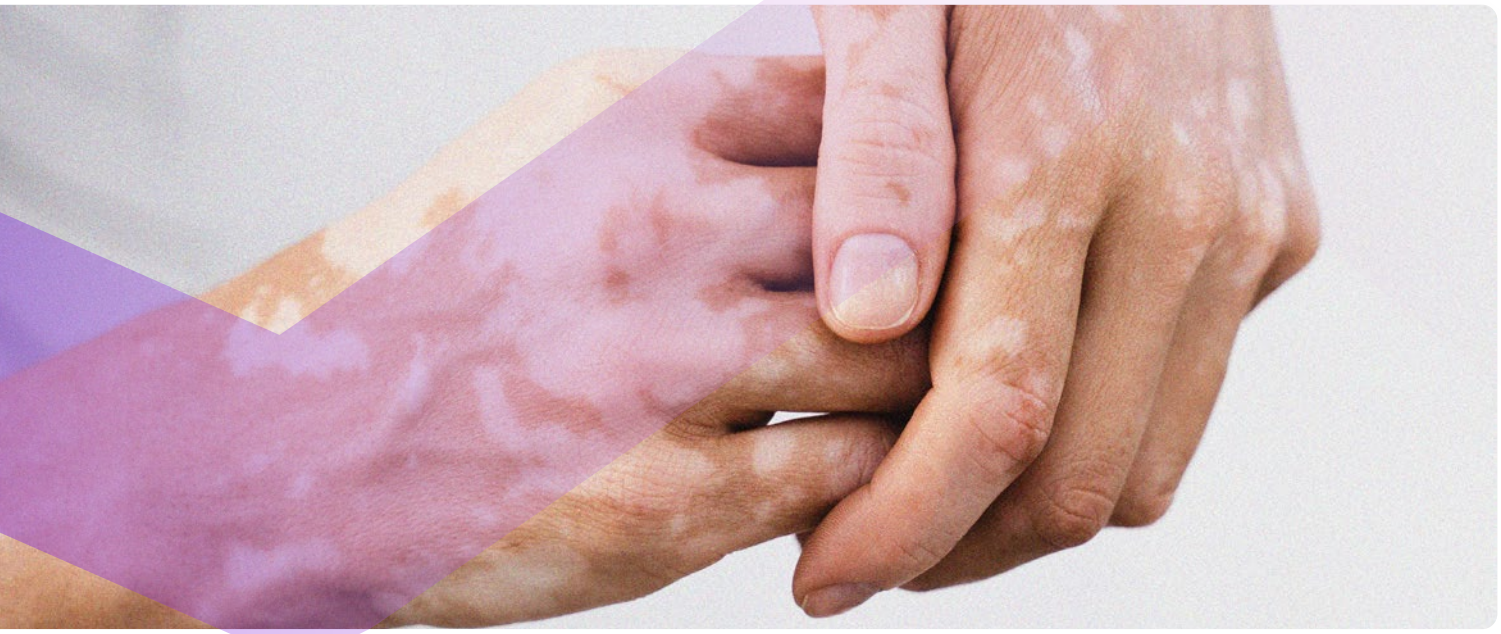
Moderate-to-severe atopic dermatitis is a condition affecting up to:

20% of adolescents

10% of adults

> **The results showed no increased risk of MACE or other cardiovascular complications in patients with AD**

The results showed no increased risk of MACE or other cardiovascular complications in patients with AD who were treated with upadacitinib or abrocitinib. These findings suggest that it is most likely safe to consider the use of these JAK inhibitors for moderate-to-severe AD, even in patients with existing cardiovascular conditions. This study provides valuable information that may help alleviate concerns about cardiovascular risks and improve the overall management of AD.



Longer Ruxolitinib Cream Use Improves Vitiligo Treatment Durability

THE RESULTS of a recent analysis of the TRuE-V long-term extension study presented at the EADV Congress 2024 suggest that longer application of ruxolitinib (RUX) cream, a JAK inhibitor, lead to more durable repigmentation in patients with vitiligo after treatment withdrawal.

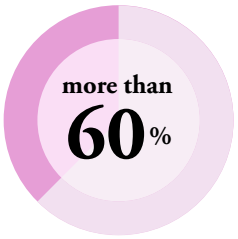
The study assessed the effect of treatment duration on maintaining facial repigmentation in patients with nonsegmental vitiligo.

In the trial, 674 patients with vitiligo covering less than 10% of their total body surface area were either treated with RUX cream or a vehicle for 24 weeks. Those who achieved significant facial repigmentation, defined as at least a 90% improvement (F-VASI90), were randomised to continue with RUX or switch to a vehicle to evaluate the durability of their repigmentation after stopping the treatment.

The results revealed that patients who used RUX cream for a longer period, up to 52 weeks, maintained their repigmentation for a median of 365 days, compared to just 91 days for those who switched to a vehicle after the initial 24 weeks of treatment. Furthermore, more than 60% of patients who used RUX cream for the full 52 weeks maintained their facial repigmentation for at least 6 months, compared to only 18% of those who stopped after 24 weeks.

Treatment-related side effects were minimal, with the most common being application site reactions, such as acne and skin irritation. None of which led to treatment discontinuation.

The study concluded that continued use of RUX cream beyond achieving facial repigmentation may offer patients with vitiligo longer-lasting results. This suggests that extending the duration of treatment could be beneficial for maintaining the positive effects of the cream, particularly in those who achieve early repigmentation.



of patients who used RUX cream for the full 52 weeks maintained their facial repigmentation for at least 6 months

> **Patients who used RUX cream for a longer period, up to 52 weeks, maintained their repigmentation for a median of 365 days**

Proteomic Biomarkers of Early, Late, and Nonresponses to Dupilumab in Atopic Dermatitis

RESEARCHERS have identified that there are distinct systemic biomarker profiles linked to the timing and maintenance of dupilumab response in patients with moderate-to-severe atopic dermatitis (AD).

Whilst dupilumab is an effective treatment for moderate-to-severe AD, prior research has demonstrated that fewer than 50% of patients achieve complete or near-complete clearance within 16 weeks of dupilumab use. Therefore, researchers aimed to identify biomarkers associated with early response, late response, nonresponse, and sustained response to dupilumab, to explore the timing and maintenance of dupilumab responses in patients.

The study, presented at the EADV Congress 2024, included 67 patients with moderate-to-severe AD treated with dupilumab, of whom, 39 were classed as early responders, 11 as late responders, and 17 as non-responders. Patients were evaluated at two follow-up visits (FU1 and FU2), with an average follow-up period of 8.9 months. Clinical scores and serum samples were collected at each visit, and proteomic analysis was performed using OLINK technology. Early responders achieved an investigator global assessment (IGA) of 0/1 or a ≥2-point reduction from baseline at both follow-ups, whereas late responders met the criteria at FU2 only, and non-responders did not meet the response criteria and/or experienced treatment dissatisfaction or adverse events. Differentially expressed proteins were defined by a fold-change >1.3 and p<0.05.

Late responders showed a 45% improvement in proteomic dysregulation from FU1 to FU2

> **Fewer than 50% of patients achieve complete or near-complete clearance within 16 weeks of dupilumab use**

The results revealed that at baseline, there were no significant differences between the groups in terms of patient characteristics or clinical severity. Additionally, early responders displayed a similar proteomic profile to healthy controls at both follow-up visits, whilst late responders showed a 45% improvement in proteomic dysregulation from FU1 to FU2, with upregulation of many Th1, Th2, Th17/22, and T cell activation/migration/dendritic cell pathways in FU1, and subsequent downregulation/normalisation at FU2. Whereas, in non-responders, there was a worsening of their blood proteome, with key Th1-related biomarkers, including CXCL9 and CXCL10, remaining significantly elevated at both follow-ups. Spearman analysis revealed positive correlations between clinical improvements and changes in blood biomarkers, particularly those involved in T cells, dendritic cells, natural killer cells, and Th2 pathways (R≥0.35; p<0.05).

The results of the study demonstrate that there are distinct biomarker profiles linked to the timing and maintenance of dupilumab responses in patients with AD. Specifically, whilst early responders show early and stable proteomic normalisation, late responders show gradual changes in Th1, Th2, and Th17/22 pathways, and non-responders demonstrate persistent dysregulation. This highlights potential biomarkers that could guide more personalised treatment strategies in clinical practice. Future research should explore targeted interventions for non-responders to improve outcomes.

Familial Hidradenitis Suppurativa Linked to Metabolic Syndrome Risk

HIDRADENITIS suppurativa (HS), also known as acne inversa, is characterised by the formation of painful nodules and fistulas, which can lead to scarring, and is driven by key cytokines such as TNF-α, IL-17, and IL-1, similar to other inflammatory skin conditions, such as psoriasis.

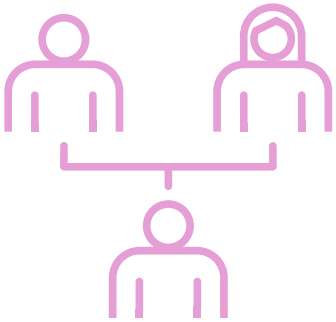
In these diseases, there is often a higher risk of metabolic syndrome, which includes conditions like hyperlipidaemia, cardiovascular disease, and Type 2 diabetes. However, the link between familial HS and the development of these metabolic conditions remains largely underexplored.

A meta-analysis, presented at the EADV Congress 2024, gathered data from two studies, EpiCAi and Batman, to generate a cohort of 236 participants, of whom 166 were female and 70 were male. Approximately 25.8% of the participants reported a family history of HS, while the remaining 74.2% had sporadic cases. Notably, the age of onset was earlier in those with a familial predisposition (20.4 years on average) compared to sporadic cases (23.6 years); however, diagnosis was delayed by about 4 years in familial cases, possibly due to self-management.

While the severity of the disease was similar between familial and sporadic cases, patients with a family history of HS had a significantly higher risk of metabolic complications. The odds ratios for hyperlipidaemia, cardiovascular disease, and diabetes were 2.36, 2.99, and 1.76, respectively, for familial cases compared to sporadic cases. This increased risk was independent of other factors such as smoking or BMI, which were similar across both groups.

The study found that patients with HS and a positive family history face a significantly higher risk of developing metabolic syndrome. The earlier onset of the disease and delayed diagnosis in familial cases highlight the need for careful cardiovascular monitoring and early intervention in these patients. This emphasises the importance of targeted care for those with a familial predisposition to HS.

> **The study found that patients with HS and a positive family history face a significantly higher risk of developing metabolic syndrome**



Approximately 25.8% of the participants reported a family history of HS

Efficacy and Safety of the IRAK4 Inhibitor Zabedosertib in Moderate-to-Severe Atopic Dermatitis

THE PHASE IIa DAMASK study assessed the efficacy and safety of zabedosertib, an oral IRAK4 inhibitor, in adult patients with moderate-to-severe atopic dermatitis (AD). Efficacy and safety data from this study were presented at the EADV Congress 2024.

The double-blind, placebo-controlled trial included 77 participants from seven countries who had an insufficient response to topical corticosteroids. Patients received either zabedosertib or placebo for 12 weeks alongside daily use of emollients. The primary endpoint was the Eczema Area and Severity Index (EASI)-75 response at Week 12, with secondary endpoints including changes in body surface area affected, pruritus scores, and validated investigator assessments.

The results showed no significant difference between zabedosertib and placebo in the primary or secondary efficacy measures. EASI-75 responses were 32.3% for zabedosertib and 37.4% for placebo. Similar non-significant results were observed for investigator assessments, pruritus scores, and body surface area changes. Additionally, biomarker analysis did not show a therapeutic effect of zabedosertib.

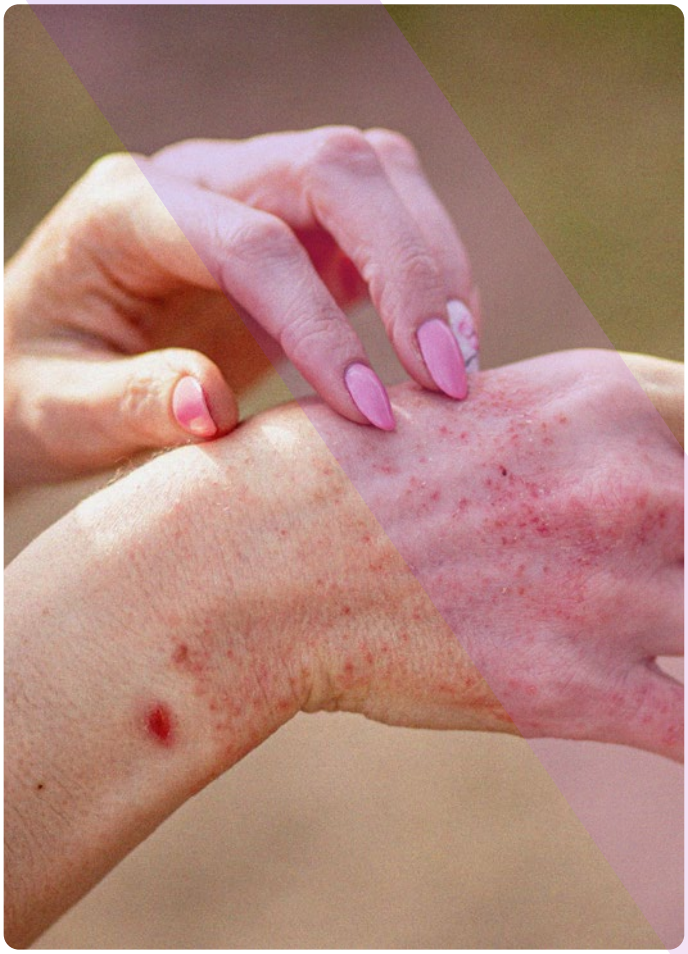
In terms of safety, 44.2% of patients in the zabedosertib group experienced treatment-emergent adverse events, compared to 28% in the placebo group, with nasopharyngitis being the most common. No serious adverse events or safety concerns were reported.

In conclusion, while zabedosertib was well tolerated, it did not demonstrate efficacy in treating moderate-to-severe AD. The findings suggest that targeting IRAK4 may not be a viable strategy for AD, though it may still hold potential for other immune-mediated conditions.

EASI-75 responses were:

32.3% for zabedosertib

37.4% for placebo



> **44.2% of patients in the zabedosertib group experienced treatment-emergent adverse events, compared to 28% in the placebo group**

New CAR-T Therapy Shows Promise for Patients with Refractory Lupus

A NEW allogeneic CAR-T therapy targeting CD19+ B cells presented at the EADV Congress 2024 has demonstrated promising results for patients with refractory systemic lupus erythematosus (SLE), offering hope for those who have not responded to traditional treatments.

The study evaluated the safety and efficacy of BRL-303, a CD19-targeted CAR-T therapy developed from healthy donor cells, in treating six patients with severe, treatment-resistant lupus.

SLE is a chronic autoimmune disease that affects multiple organs and is often treated with immunosuppressive drugs. However, many patients do not achieve remission and face significant side effects from prolonged immunosuppression. BRL-303 represents a new approach by deeply depleting CD19+ B cells, potentially resetting the immune system in patients with autoimmune diseases.

In this investigator-initiated trial, patients received BRL-303 after lymphodepletion chemotherapy, which prepares the immune system for CAR-T cell infusion. Results from the trial showed that the CAR-T cells expanded rapidly in all patients within 7 days, peaking between Days 14 and 21. Over the next 1–3 months, the therapy led to deep, sustained depletion of B cells in the bloodstream.

After a median follow-up of 6 months, all six patients showed significant clinical improvements, including reductions in disease activity scores and remission of symptoms. Proteinuria, a marker of lupus nephritis, also significantly decreased in those affected. Importantly, the safety profile of BRL-303 was favourable, with only mild side effects such as low-grade cytokine release syndrome reported, and no cases of severe infection or neurotoxicity.

These early findings suggest that BRL-303 could represent a breakthrough for patients with SLE who have not responded to current therapies. The trial is ongoing, with further research planned to explore the therapy's effects in lupus and other autoimmune diseases.

> **After a median follow-up of 6 months, all six patients showed significant clinical improvements**

Delgocitinib Cream versus Dupilumab: Comparing Eczema Treatments

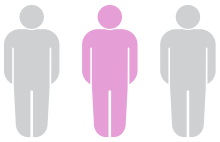
A TOPICAL, investigational pan-JAK inhibitor, delgocitinib cream, has shown notable efficacy in treating various subtypes of chronic hand eczema (CHE), including atopic hand eczema (AHE), according to research presented at the EADV Congress 2024.

The cream is well tolerated, with a favourable safety profile, making it a promising option for patients. In contrast, dupilumab, a biologic that inhibits IL-4 and IL-13 signalling pathways, is approved for moderate-to-severe atopic dermatitis (AD) treatment, including AD that affects the hands. However, no direct studies have compared the efficacy of delgocitinib and dupilumab, specifically for AHE.

To address this gap, a matching-adjusted indirect comparison (MAIC) was performed using data from the DELTA 1 and DELTA 2 trials and the LIBERTY-AD-HAFT trial. The DELTA 1 and 2 trials were Phase III studies that assessed delgocitinib cream in adults with moderate-to-severe CHE. Participants were randomised in a 2:1 ratio to receive either delgocitinib, as a dosage of 20 mg/g, or a cream vehicle twice daily for 16 weeks. The LIBERTY-AD-HAFT trial included adults and adolescents (aged 12 to under 18 years) with moderate-to-severe AD involving the hands or feet, who were treated with subcutaneous dupilumab or placebo every 2 weeks for 16 weeks.

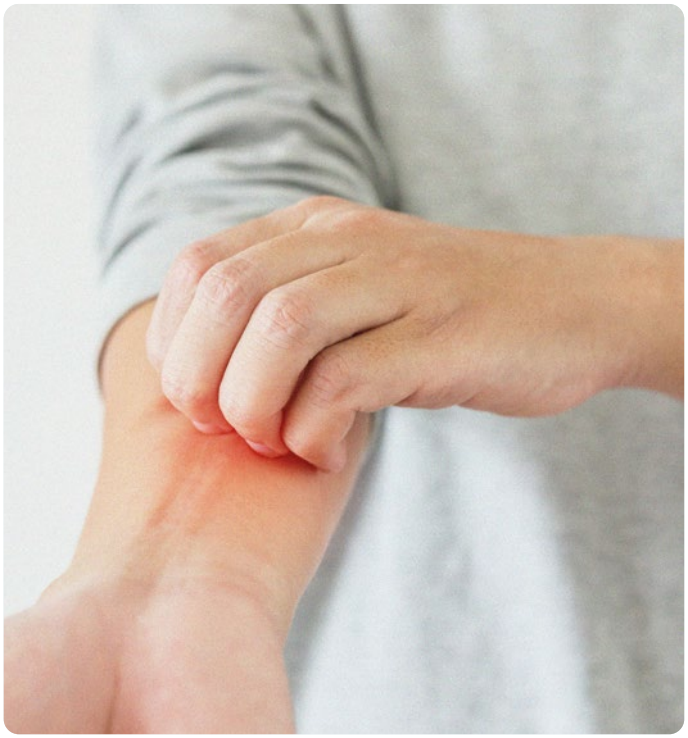
Since no direct comparisons were available, the MAIC was conducted using individual patient data from DELTA 1 and 2, and published aggregate data from LIBERTY-AD-HAFT. The LIBERTY-AD-HAFT trial included 133 participants, while DELTA 1 and 2 included 959 patients, 345 of whom had been diagnosed with AHE.

Patients with AHE as the primary subtype in the DELTA trials were weighted to match baseline characteristics, such as age, race, sex, and baseline Hand Eczema Severity Index (HECSI) scores of participants in the LIBERTY-AD-HAFT trial. Efficacy endpoints included achieving HECSI 75 and HECSI 90 and the percentage improvement from baseline at Week 16. Investigator's Global Assessment scores (IGA), IGA-CHE for DELTA trials and HF-IGA for LIBERTY-AD-HAFT, were also compared, although these scales differed in response definitions.



DELTA 1 and 2 included 959 patients, 345 of whom had been diagnosed with AHE.

The study found that topical delgocitinib demonstrated comparable efficacy to systemic dupilumab after 16 weeks in patients with AHE. However, while statistical significance was not achieved, delgocitinib may be an effective alternative for AHE treatment, warranting further investigation.



Efficacy and Safety of the TYK2 Inhibitor HS-10374 in Moderate-to-Severe Plaque Psoriasis

DATA from a Phase II trial that evaluated the efficacy and safety of HS-10374, an oral selective Tyrosine kinase 2 (TYK2) inhibitor, in treating moderate-to-severe plaque psoriasis, were presented at the EADV Congress 2024.

TYK2 is crucial for IL-12 and IL-23 signalling, which are key cytokines in psoriasis. In this randomised, double-blind, placebo-controlled study, 125 patients were assigned to three groups: HS-10374 6 mg, HS-10374 12 mg, or placebo. The treatment period lasted 12 weeks, with a 4-week follow-up.

> **125 patients were assigned to three groups: HS-10374 6 mg, HS-10374 12 mg, or placebo**

The primary endpoint was met at Week 12. The Psoriasis Area and Severity Index (PASI) 75 response rate was 28.6% for the 6 mg group and 72.1% for the 12 mg group, compared to 7.5% for the placebo group. Additional endpoints, such as static Physician's Global Assessment 0/1, PASI 50, and PASI 90, were also significantly higher in the HS-10374 groups.

Safety outcomes were similar across all groups, with slightly higher adverse event (AE) rates in the HS-10374 groups.

Treatment-related AEs and serious AEs were comparable, with one unrelated serious AE (limb trauma) in the 6 mg group and one gastrointestinal-related serious AE in the placebo group. Infections were the most commonly reported AEs, but there was no significant increase in skin-related AEs compared to placebo.

In conclusion, HS-10374 demonstrated significant efficacy in treating plaque psoriasis with a safety profile consistent with other TYK2 inhibitors. Further trials with larger populations and longer treatment durations are needed.

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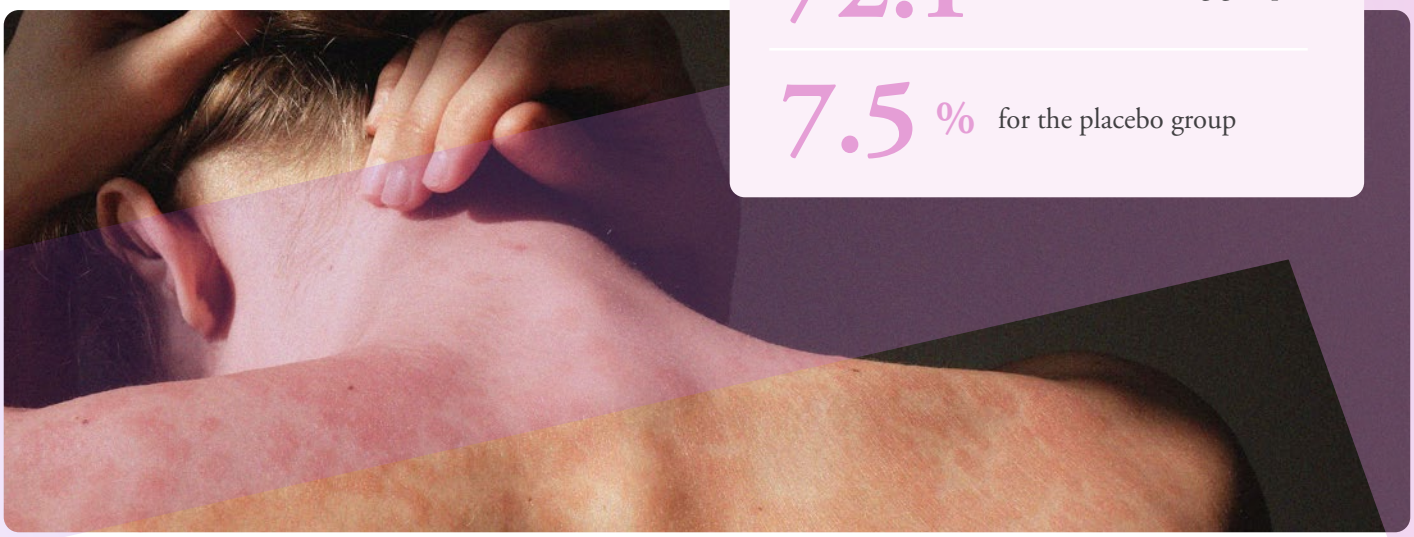
28.6 %	for the 6 mg group
72.1 %	for the 12 mg group
7.5 %	for the placebo group



JAK Inhibitor Delgocitinib Reduces Hair Loss and Inflammation in Frontal Fibrosing Alopecia

THE TOPICAL JAK inhibitor, delgocitinib, has shown to be effective for stabilising hair shedding and promoting hair regrowth in patients with frontal fibrosing alopecia (FFA), whilst reducing Th1/IFN-γ-driven inflammation in the scalp.

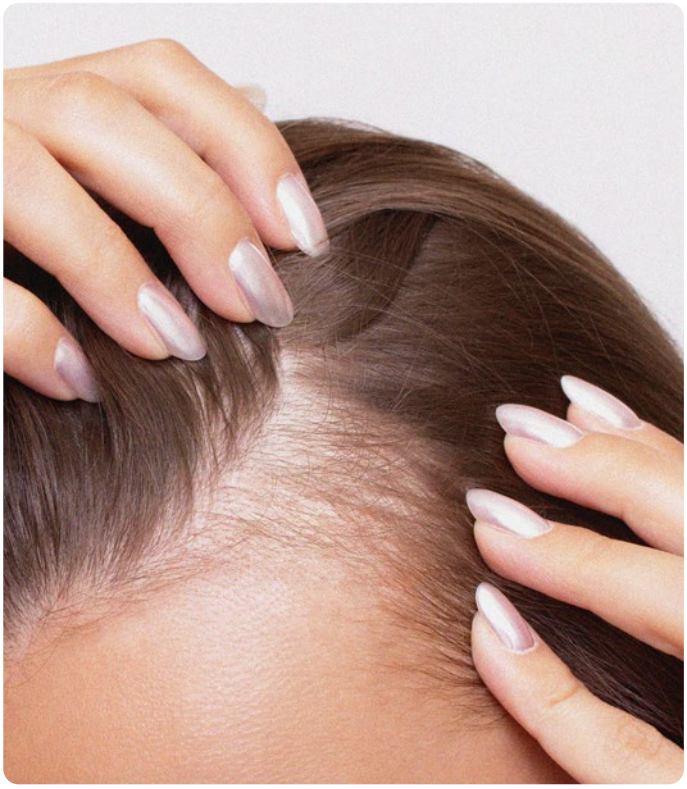
There are currently no approved or efficacious treatments for FFA, a scarring alopecia characterised by progressive frontotemporal recession which leads to permanent hair loss. This condition has an increasing prevalence, particularly in women, with prior research linking its pathogenesis to Th1/IFN-γ activation. Therefore, researchers sought to investigate the effect of the topical pan-JAK inhibitor, delgocitinib, on Th1/INF-γ-driven inflammation and clinical disease severity in FFA.

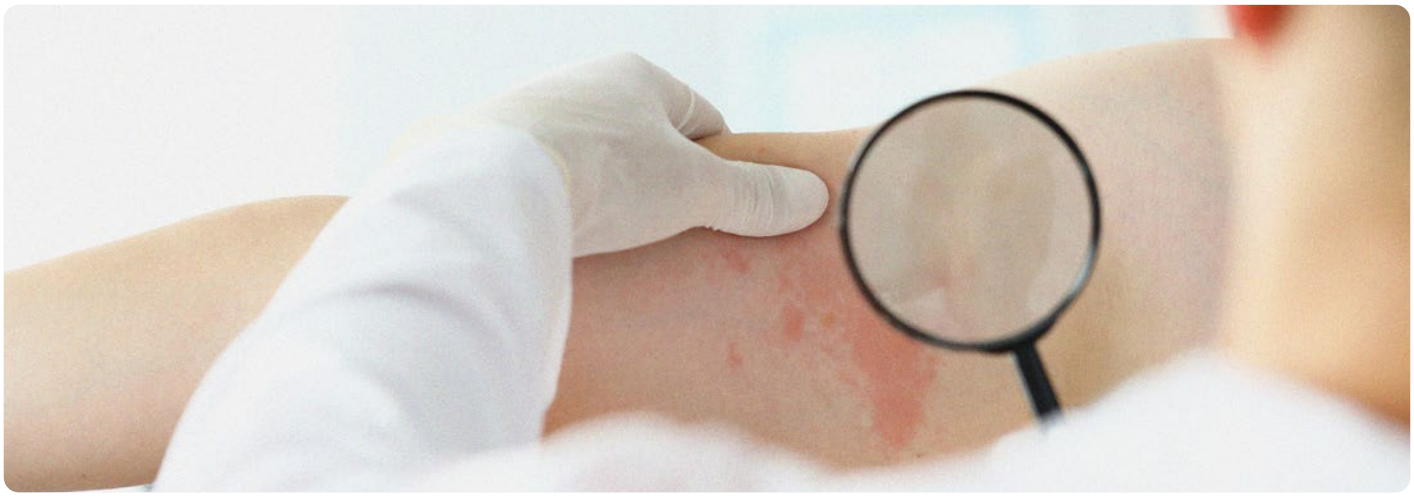
The researchers conducted a double-blind, randomised, vehicle-controlled trial with 30 patients with FFA. Participants were assigned to either receive delgocitinib cream (20 mg/g) or a matching vehicle cream twice daily for 12 weeks, followed by a 12-week open-label extension with delgocitinib for all participants. Lesional and non-lesional scalp skin biopsies were taken at baseline and after 12 weeks to assess transcriptomic changes. In addition, clinical severity scores and trichoscopic images of hair counts were monitored throughout the study.

The analysis, presented at the EADV Congress 2024, revealed a reduction in the expression of Th1/IFN-γ-related genes, including CXCL9 (–3.10; $p<0.05$), CXCL10 (–2.60; $p<0.1$), and IFN-γ (–1.49; $p=0.22$) in lesions that were treated with delgocitinib after 12 weeks. Furthermore, there was a 4% improvement in transcriptomic normalisation towards non-lesional profiles in delgocitinib-treated patients ($p<0.001$), compared to a 33% worsening in the vehicle group. Clinical severity scores, including the Lichen Planopilaris Activity Index (LPPAI) and Frontal Fibrosing Alopecia Severity Scores (FFASS), significantly improved in the delgocitinib group by Week 12 ($p=0.023$). Further improvements were seen during the open-label extension, where all subjects treated with delgocitinib obtained some degree of hair regrowth. Trichoscopy analysis revealed an increase in hair density and follicular units in the delgocitinib group, whereas reductions were seen in the vehicle group. Furthermore, delgocitinib was well-tolerated, with no significant safety concerns.

> **Trichoscopy analysis revealed an increase in hair density and follicular units in the delgocitinib group**

In conclusion, delgocitinib demonstrated promise as a treatment for FFA, by reducing inflammation and showing signs of hair regrowth. Further studies are needed to confirm the long-term efficacy of delgocitinib, and to better define its role in clinical practice for FFA management.





Ruxolitinib Cream Shows Long-Term Safety in Paediatric Dermatitis

THE TRuE-AD3 study, presented at the EADV Congress 2024, evaluated the long-term safety and efficacy of ruxolitinib (RUX) cream in children aged 2–11 years with atopic dermatitis (AD).

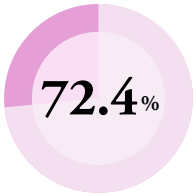
In this Phase III study, children with mild-to-moderate AD applied either 0.75% or 1.5% RUX cream or a vehicle cream twice daily for an initial 8-week period. Following this, patients who initially used RUX cream continued as-needed treatment for 44 weeks. Those initially assigned to the vehicle cream were rerandomised to one of the two RUX cream concentrations.

> **The study demonstrated that RUX cream at both strengths was safe and effective over 52 weeks**

Safety was a primary focus, with no new adverse events reported during the long-term period. The study demonstrated that both concentrations of RUX cream were well tolerated, with a low rate of treatment-emergent adverse events (TEAEs). The most common TEAEs were upper respiratory tract infections and nasopharyngitis, although these were generally mild. Application site reactions were also minimal, affecting only 5.3% of participants, and no TEAEs indicated systemic absorption of the drug, consistent with low plasma levels of RUX.

The results showed the efficacy of the RUX cream, with substantial improvement in disease control in these patients who showed significantly better outcomes than those using the vehicle cream at the 8-week mark. Half of the patients using the RUX cream at a strength of 0.75% and 72.4% of those using 1.5% RUX cream achieved clear or almost clear skin, compared to only 24.5% in the vehicle group. These improvements were sustained or even enhanced by Week 52, with around 72–79% of patients achieving clear or almost clear skin regardless of the RUX cream strength. Additionally, the affected body surface area was notably reduced for patients on RUX cream, with a reduction maintained throughout the study.

The study demonstrated that RUX cream, at both strengths, was safe and effective over 52 weeks, significantly reducing AD symptoms and maintaining a low affected body surface area. This provides encouraging evidence for the long-term use of RUX cream as an effective treatment for managing AD in young children.



of those using 1.5% RUX cream achieved clear or almost clear skin