AAD 2024

DO NOT MISS HIGHLIGHTS IN PSORIATIC DISEASE

MARCH 2024

NEWSLETTER

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Y-GRAPPiANs

Young Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Y-GRAPPA members prepared this Newsletter. It highlights some of the very interesting abstracts on psoriatic disease that will be presented at the 2024 AAD Annual Meeting in San Diego.

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Perceived stress can trigger psoriatic lesions in human skin in vivo, which can be suppressed by aprepitant

Aviad Keren

Poster ID: 53005

https://aad-eposters.s3.amazonaws.com/AM2024/poster/53005/Perceived+stress+can+trigger+psoriatic+lesions+in+human+skin+in+vivo+which+can+be+suppressed+by+aprepitant.pdf

The relationship between psychogenic stress and psoriasis exacerbation is a commonly observed clinical phenomenon, yet its conclusive evidence is lacking.

To investigate this relationship, the researchers conducted a study on humanized psoriasis mice by inducing neurogenic skin inflammation using sonic (sound) stress. They injected 25 mice with grafted skin with IL-2-induced PBMCs one month after the grafting process. Five days after a psoriatic skin lesion appeared, they treated the mice with dexamethasone for three days. Then, they exposed the mice to 24 hours of sonic stress. They obtained the human skin grafts and the perigraft mouse skin at 14 days and assessed them for inflammation and neuronal activity markers.

The results showed that sound stress exacerbated psoriasis in human skin, as evidenced by the histopathological features of the disease and a significant increase in psoriatic markers such as hβ2-defensin, S100A7, c-KIT, Tryptase, K16, Ki67, HLA-DR, ICAM-1, CD1d, CXCL10, CD3, CD8, CD11c, IL-22, IL-15, IL-17A/F, IFN-γ, TNFα, ILC3, plasmacytoid DC and NKG2D+/ CD56+cells, as compared to sham-stressed mice and stressed mouse skin.

Neurogenic skin inflammation markers such as NGF, NK1-R, and substance P were also significantly increased.

Moreover, aprepitant, a neurokinin-1 receptor antagonist, prevented the reappearance of psoriatic lesions after stress exposure and reduced the expression of inflammatory and neurogenic markers.

WHY IMPORTANT?

*First definitive evidence that stress can induce psoriatic lesions in human skin in vivo, probably led by substance P-induced neurogenic inflammation.

*Aprepitant, an FDA-approved anti-emetic drug, might hold therapeutic promise in reducing stress-induced psoriasis flare-ups.

POLLING QUESTION

How often do you encounter psoriasis patients whose symptoms are exacerbated by psychogenic stress?

Normalization of molecular signatures associated with pruritis in plaque psoriasis correlate with itch resolution following bimekizumab treatment

Ioana Cutcutache

Presentation:

Monday, March 11 2:05 PM –

San Diego Convention Center (Upper Level, Sails Pavilion, Poster Center 1)

Poster ID: 52693

https://aad-eposters.s3.amazonaws.com/AM2024/poster/52693/Normalization+of+molecular+signatures+associated+with+pruritis+in+plaque+psoriasis+correlate+with+itch+resolution+following+bimekizumab+treatment.pdf

(Disclosures: Authors are employees and shareholders of UCB Pharma.)

Some patients with plaque psoriasis suffer from severe pruritus, which can substantially affect their quality of life.

In phase 3 clinical trials, patients treated with the IL17A/F antagonist bimekizumab had a superior reduction in pruritus compared to other active treatments or placebo, according to a comparison of P-SIM item 1 (itching) scores.

In this study, patients received bimekizumab 320mg at weeks 0 and 4. Lesional and non-lesional skin biopsies were obtained at weeks 0 and 8. To assess pruritic signature, the researchers used the Gene Set Variation Analysis (GSVA) and *limma* frameworks.

The pruritic signature was mostly expressed in mast cells and keratinocytes, with upregulation of specific mediators such as KLK8 and TRPV3.

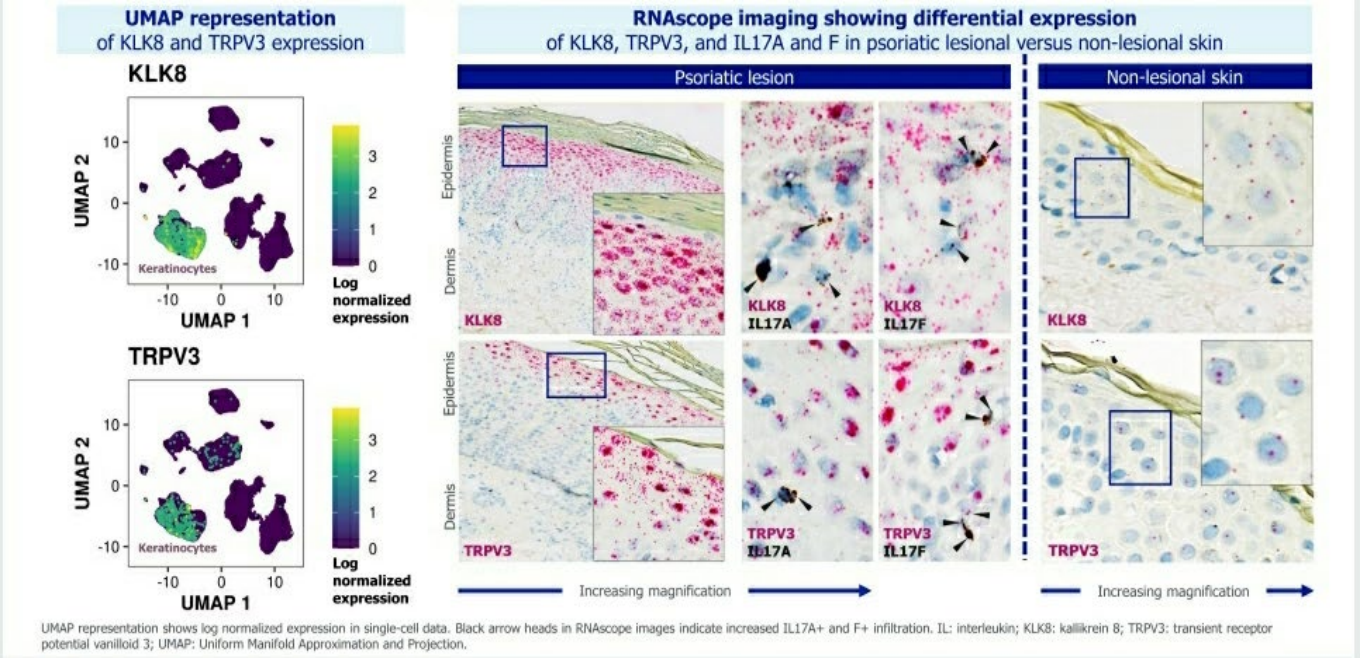
After two bimekizumab doses, the pruritic signature returned to non-lesional levels. Pruritus modulators such as KLK6/8/14, TRPV3, and HRH2/3 also normalized after treatment.

WHY IMPORTANT?

This study provides insights into the pathways leading to itch resolution after psoriasis treatment.

POLLING QUESTION

Could the fact that only some psoriasis patients experience itching be an indicator for personalized medicine-based treatment options in the future?



UMAP representation shows log normalized expression in single-cell data. Black arrow heads in RNAscope images indicate increased IL17A+ and F+ infiltration. IL: interleukin; KLK8: kallikrein 8; TRPV3: transient receptor potential vanilloid 3; UMAP: Uniform Manifold Approximation and Projection.

Short-chain fatty acid ameliorates imiquimod-induced skin and systemic inflammation and alters gut microbiota in mice: a metagenome association analysis

Yi-Ju Chen

Presentation:

Sunday, March 10 3:35 PM

San Diego Convention Center (Upper Level, Sails Pavilion, Poster Center 2)

Poster ID: 50200

https://aad-eposters.s3.amazonaws.com/AM2024/poster/50200/Short-chain+fatty+acid+ameliorates+imiquimod-induced+skin+and+systemic+inflammation+and+alters+gut+microbiota+in+mice+a+metagenome+association+analysis.pdf

The researchers aimed to investigate the effects of short-chain fatty acid (SCFA) supplementation on psoriasis.

They carried out a metagenome-wide association study on imiquimod-treated mice, dividing them into two groups - one given SCFA and the other given IL17 antagonists.

Both the mice treated with SCFA and IL17 antagonists showed a decrease in the skin thickness, spleen weight, and serum IL-17A/F levels. However, the mice given SCFA showed greater microbial diversity, leading to increased glycan breakdown, phenylalanine metabolism, and xylene breakdown.

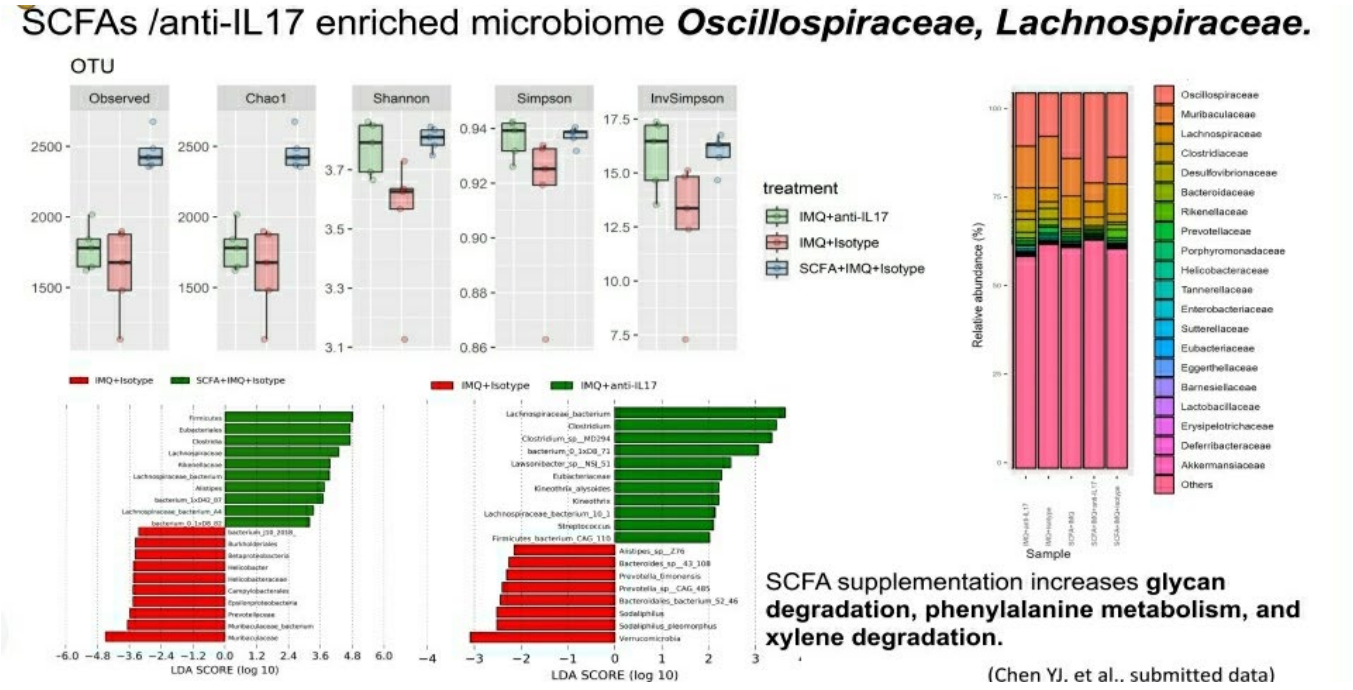
These results suggest that SCFA may improve systemic and skin inflammation by gut microbiome regulation which then affects inflammatory and metabolic signalling.

WHY IMPORTANT?

Gut microbiome modulation may help mitigate skin and systemic inflammation in patients with psoriasis.

POLLING QUESTION

How much do you think treatment options targeting the gut or skin microbiota will change the psoriasis treatment landscape in the future?



CLINICAL

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- Y-GRAPPA member, newsletter committee member
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Comparative Effectiveness of Biologic Classes in Clinical Practice: Month 12 Outcomes from the International Observational Psoriasis Study of Health Outcomes (PSoHO)

Saakshi Khattri

Time of presentation- Monday, March 11 1:15 PM - San Diego Convention Center (Upper Level, Sails Pavilion, Poster Center 1)

Abstract #51784

Link to abstract- https://eposters.aad.org/abstracts/51784

PSoHo is a 3 year, international, prospective, real- world data on treatment of psoriasis with various biologics. The study aimed to assess long term effectiveness of different biologics in moderate to severe psoriasis over 12 months.

PSoHo enrolled adult patients (age ≥ 18 years) with moderate to severe psoriasis due to initiate or switch biologic therapy as part of routine care. They compared the biologic classes anti-IL17A/RA (ixekizumab, secukinumab and brodalumab), anti-IL23p19 (guselkumab, tildrakizumab and risenkizumab), anti-IL12/23p40 (ustekinumab) and anti-TNFα (adalimumab, certolizumab, etanercept and infliximab). They assessed PASI 100 response at week 12, month 6 and month 12.

Baseline characteristics were similar in the cohorts except for significantly fewer patient with PsA being switched to / initiated on anti-12/23p40 or anti-IL23p19 biologics. Also, significantly more patients had prior treatment with biologics before switching to an anti-TNFα or anti-IL23p19 biologic.

Unadjusted response rate for achieving PASI 100 was higher in the anti-IL17A/RA cohort at all time points. The only exception was comparable effectiveness of anti-IL17A/RA and anti-IL23 p19 at month 12. Similarly, durability of treatment (sustained effectiveness) was higher for anti-IL17A/RA compared to the other biologics cohorts.

WHY IMPORTANT?

This study gives a head-to-head comparison between biologics classes in a real-world setting.

It demonstrates effectiveness and durability of anti-IL17A/RA agents compared to other biologic classes.

POLLING QUESTION

Which biologics class would you prefer in moderate to severe psoriasis as a first choice ?

GUIDE trial (part 3): Following guselkumab withdrawal and a long treatment-free period, disease control is rapidly regained upon re-treatment in psoriasis super-responders

Khusru Asadullah

Abstract #49730

Link to abstract- https://eposters.aad.org/abstracts/49730

GUIDE is an ongoing phase 3b RCT comparing treatment effects of the IL-23p19 antagonist guselkumab in patients with short (≤2 years) or longer (>2 years) duration of psoriasis. Some participants were super-responders (SRe), defined as PASI = 0 at week 20 and week 28. This abstract presents data on the effect of guselkumab withdrawal in SRe and subsequent response to re-treatment.

SRe with PASI <3 at week 68 were withdrawn from guselkumab. Those who had a relapse with PASI >5 at week 68 were restarted on guselkumab at week 0, week 8 and week 16 (R0, R8 and R16).

Of the 273 patients who were withdrawn, 186 relapsed at week 68 and restarted guselkumab. Median treatment free duration was 302 days. Patients with disease duration ≤ 2 years were more likely to remain treatment free.

On re-initiation of guselkumab, 75.8% achieved disease control (PASI < 3) at week 8, and 92.5% at week 24. Prior dosing intervals (q8W / q16W) and body weight (≤90 kgs or >90kgs) did not impact the ability to regain disease control. Mean PASI, DLQI and PSSD showed rapid improvement on retreatment (even after a single dose).

Patients who achieved PASI = 0 at time of withdrawal, had more chances of being treatment free and had better response when restarted on guselkumab .

WHY IMPORTANT?

This study highlights the importance of attaining complete disease remission before attempting withdrawal.

It enforces that relapse rate is high post withdrawal, but retreatment can regain disease control in super-responders.

POLLING QUESTION

Should guselkumab be withdrawn in patients who achieved PASI =0 at week 20 and week 28 (super-responders) ?

Validation of the IDEOM MSK-Q

Gretchen Ball

Abstract #50347

Link to abstract- https://aad-eposters.s3.amazonaws.com/AM2024/poster/50347/Validation+of+the+IDEOM+MSK-Q.pdf

IDEOM (International Dermatology Outcome Measure) MSK – Q is a patient reported musculoskeletal questionnaire to assess the intensity of musculoskeletal symptoms and fatigue, along with the impact on patients' health related quality of life. It includes 9 items subdivided into 3 groups- "intensity of MSK symptoms", "impact of MSK symptoms" and " intensity of fatigue ".

This observational, cross-sectional multi-centre study will validate the IDEOM MSK-Q in adult patients (age ≥ 18 years) with psoriasis and PsA. Patients will be divided into 2 groups with 50 patients in each group; Group-1 – patients with psoriasis but no arthritis , Group- 2 – patients with PsA (confirmed by a rheumatologist).

This study hypothesizes to find moderate to strong correlation between IDEOM MSK-Q and other similar instruments.

The clinical assessment of psoriasis will include PASI, BSA, physician global assessment (PGA) and presence of nail psoriasis. The clinical assessment of PsA will include tender and swollen joints counts (TSJC) over 66/68 joints, Leeds enthesitis index, dactylitis count and the presence of inflammatory back pain. Patients in both groups will be required to fill IDEOM-MSK Q and PEST (Psoriasis Epidemiology Screening). A blinded rheumatologist will document diagnosis of PsA. Sensitivity, specificity, ROC and area under ROC for IDEOM MSK Q will be analysed. The reliability of the instrument will be tested by asking participants to redo the IDEOM MSK Q after 2-10 days. Only patients who are stable will be analysed .

WHY IMPORTANT?

A new clinical tool to assess the intensity and impact of MSK symptoms and fatigue in patients with psoriasis PsA is very much needed as perspective of same may differ from physician and patient's point of view.

POLLING QUESTION

Is there a need for a validated tool to assess intensity and impact of musculoskeletal symptoms in patients with psoriasis and PsA?

TREATMENT

- Nicolette John
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Comparing the Effect of Risankizumab versus Apremilast on Psoriasis Symptoms, Treatment Satisfaction, and Health-Related Quality of Life from the Phase 4 IMMpulse Study

Andreas Pinter

Time of Presentation

Sunday, March 10th

Poster ID: 50250

https://eposters.aad.org/abstracts/50250

The IMMpulse phase-4 study (NCT04908475) was a multicenter, randomized, open-label, efficacy assessor-blinded, active-comparator clinical trial designed to evaluate the efficacy of risankizumab (anti-IL23p19) compared to apremilast (anti-PDE4) in treating systemic-eligible adult patients with moderate plaque psoriasis.

The study included 118 patients receiving risankizumab and 234 patients receiving apremilast, with the treatment period spanning 16 weeks. The study focused on comparing patient-reported outcomes, including the Psoriasis Symptoms Scale (PSS), Treatment Satisfaction Questionnaire for Medication version-9 (TSQM-9), and Dermatology Life Quality Index (DLQI).

A higher proportion of risankizumab-treated patients achieved significant symptom improvement, higher treatment satisfaction levels, and better quality of life scores at both the 4-week and 16-week marks compared to those receiving apremilast. These results suggest risankizumab may offer a more effective treatment than apremilast for adult patients with moderate plaque psoriasis.

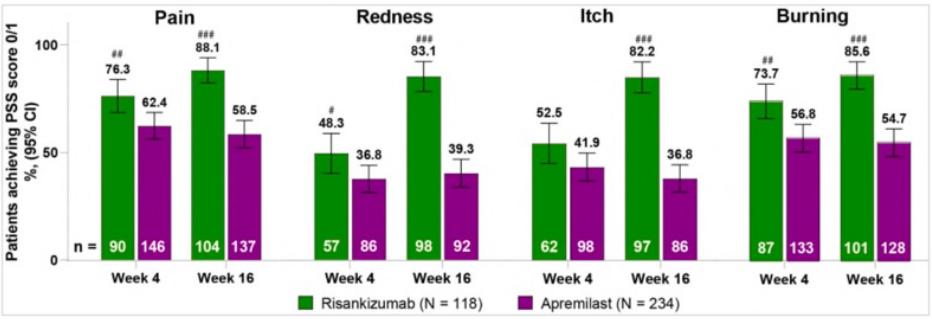
WHY IMPORTANT?

This study demonstrates that risankizumab could be a preferable treatment option to apremilast for many patients.

POLLING QUESTION

Which outcome measurement in the IMMpulse phase-4 study do you think is the most important indicator of treatment success for moderate plaque psoriasis?

Figure 1. Responder analyses of Psoriasis Symptom Scale (PSS) items



The PSS consists of four items assessing severity of pain, itching, redness, and burning during the past 24 hours; the 5-point severity scale is as follows: 0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe. ###, ##, #, nominal significance at 0.001, 0.01, 0.05 level, respectively compared with apremilast

Clinical Efficacy of TAK-279, a Highly Selective Oral Tyrosine Kinase 2 (TYK2) Inhibitor, Is Associated with Modulation of Disease and TYK2 Pathway Biomarkers in Patients with Moderate-to-Severe Psoriasis

James G Krueger

Time of Presentstion

Sunday, March 10th

Poster ID: 50250

Poster ID: 50378

https://eposters.aad.org/abstracts/50378

TYK2 is involved in the signalling of cytokines implicated in psoriasis pathogenesis and TAK-279 is a selective oral TYK2 inhibitor. This phase 2b randomized, double-blind, placebo-controlled trial examined the impact of TAK-279 on disease biomarkers and clinical outcomes over 12 weeks in patients with moderate-to-severe psoriasis.

Patients received either a placebo or TAK-279 at varying doses (2 mg, 5 mg, 15 mg, or 30 mg). The study utilized biopsies and serum samples to analyze changes in disease markers like epidermal thickness, keratinocyte proliferation, and IL-23/Th-17 pathway activity. The key findings were that the TAK-279 treatment led to significant improvements in PASI scores, reductions in keratin 16 expression, and decreased levels of IL-17A and IL-17F, both in skin lesions and serum. These changes corresponded with clinical and histologic improvement, without a clear dose-dependence in adverse event frequency.

The study concluded that TAK-279 effectively modulates psoriasis and TYK2 pathway biomarkers, with larger studies planned to confirm the findings.

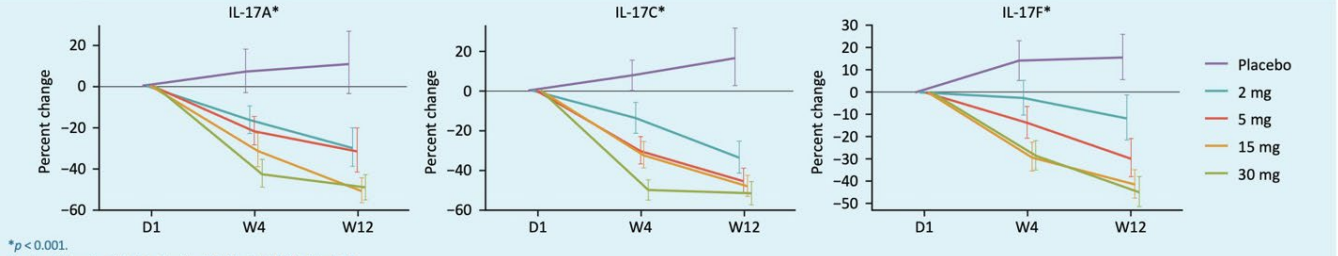
WHY IMORTANT?

By demonstrating strong correlations between clinical improvements and biomarker modulation, the study improves the understanding of psoriasis pathophysiology and hints at the future of personalized medicine for this chronic condition. The findings could lead to changes in clinical practice and improve patient quality of life.

POLLING QUESTION

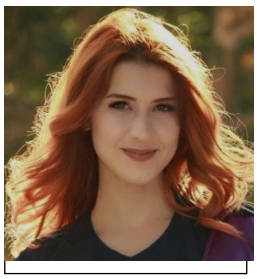
How does TAK-279, as studied in the phase 2b clinical trial, impact patients with moderate-to-severe psoriasis?

FIGURE 4. TAK-279 TREATMENT WAS ASSOCIATED WITH DOSE- AND TIME-DEPENDENT REDUCTIONS IN SERUM IL-17A, IL-17C AND IL-17F.



*$p < 0.001$.
D1, day 1 (baseline); IL, interleukin; W4, Week 4; W12, Week 12.

TREATMENT



- Ayşenur ŞAM SARI
- Dermatology Specialist at Kolmed Private Hospital, Amasya, Turkey
- Research focus: Hair and Nail Diseases

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Efficacy of Risankizumab Versus Apremilast Among Patients with Scalp or Nail Psoriasis from the Phase 4 IMMpulse Study

Linda Stein Gold MD

Time of presentation

Sunday, March 10

Poster ID: 50251

Link to abstract

https://eposters.aad.org/abstracts/50251

Psoriasis affecting the scalp or nails poses significant challenges in management due to its impact on patients' quality of life. This study aimed to compare the efficacy of two treatments, risankizumab and apremilast, in patients with baseline scalp or nail psoriasis.

The IMMpulse study (see page 8), a phase 4 multicenter trial, enrolled systemic-eligible adult patients with moderate chronic plaque psoriasis. Participants were randomized to receive either risankizumab or apremilast over 16 weeks. Outcomes including skin clearance, quality of life, and treatment satisfaction, were assessed at weeks 4, 16, and 52.

Results demonstrated that risankizumab exhibited superior efficacy compared to apremilast in achieving skin clearance, improving quality of life, and enhancing treatment satisfaction by week 16.

These findings highlight the efficacy of risankizumab as a preferred treatment option for patients with scalp or nail psoriasis, particularly those with significant involvement in these high-impact areas.

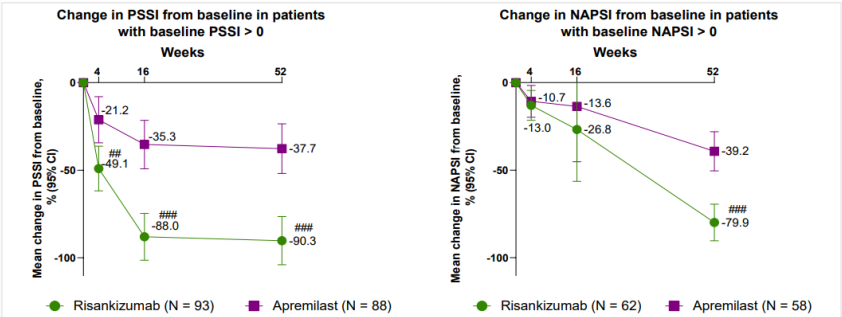
WHY IMPORTANT?

At week 16, risankizumab has shown superiority over apremilast in terms of skin clearance, quality of life improvement, and treatment satisfaction among patients with baseline scalp or nail psoriasis.

POLLING QUESTION

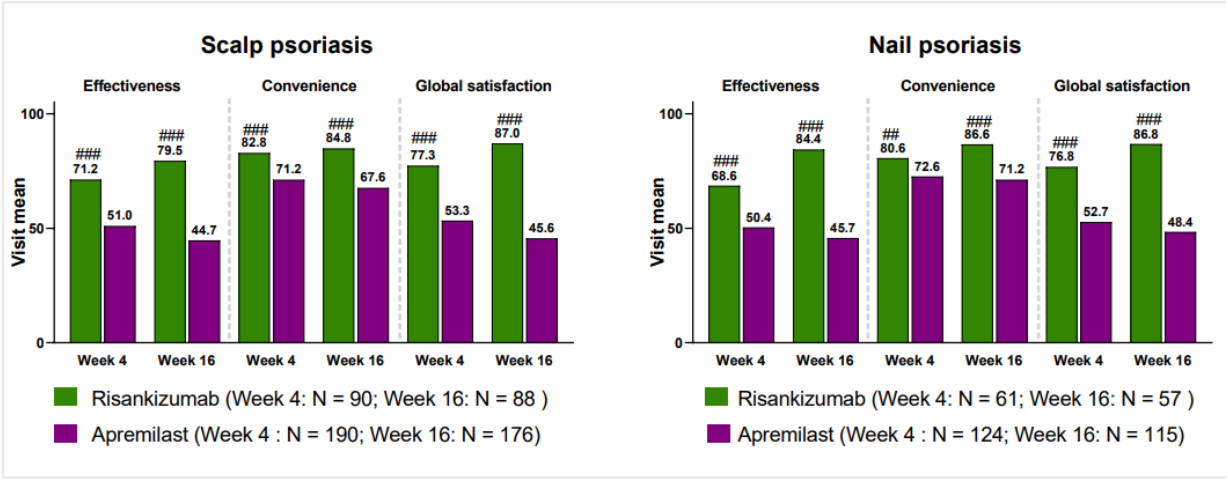
What treatment do you believe would be more effective for patients with baseline scalp or nail psoriasis: risankizumab or apremilast?

Figure 1. Improvement in PSSI and NAPSI in patients treated with risankizumab vs. apremilast from week 0 to 52



##, ###, Nominal P-value 0.01, 0.001; The missing data was handled using the Last Observation Carried Forward (LOCF) imputation method

Figure 4. Mean treatment satisfaction scores with risankizumab vs. apremilast treatment



##, ###, Nominal P value 0.01, 0.001. Non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 was used

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