EADV 2023

DO NOT MISS HIGHLIGHTS IN PSORIATIC DISEASE

OCTOBER 2023

NEWSLETTER

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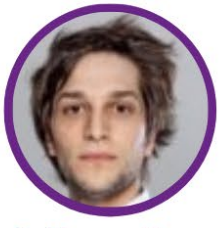
Y-GRAPPiAns
Young Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Y-GRAPPA members prepared this Newsletter. It highlights some of the very interesting abstracts on psoriatic disease that will be presented at the 2023 EADV congress in Berlin.

Rachel Grynszpan
LEADER

Gizem Ayan
COORDINATOR

Hanna Johnsson
COORDINATOR



Guilherme Muzy
BASIC SCIENCE HIGHLIGHTS

Dimitri Luz
BASIC SCIENCE & CLINICAL HIGHLIGHTS

Arianna Zhang
TREATMENT HIGHLIGHTS

BASIC SCIENCE

- Guilherme Muzy, MD
- Private practice and ABC School of Medicine, Brazil
- Y-GRAPPA member, participates in the Education Committee and Slide Library Project
- Research focus: Immune-mediated skin diseases such as PsA, AD, AA and HS

A pilot genome-wide association study identifies novel markers of metabolic syndrome in patients with psoriasis

Seung-Min Oh, Su-Kang Kim, Hye-Jin Ahn, Ki-Heon Jeong

Abstract #1196

Poster ID P2355
e-Poster Hall, Wednesday 11 Oct

Psoriasis is associated with the metabolic syndrome with multiple shared inflammatory and cytokine-mediated pathways. However, the pathogenic mechanism of the association is complex and not fully understood.

The aim of this study was to investigate for genetic associations.

Genotyping of 95 patients with psoriasis with (n=38) and without (n=57) metabolic syndrome identified 76 gene polymorphisms which conferred an increased risk of metabolic syndrome in this population. The strongest association between metabolic syndrome and psoriasis were with the single nucleotide polymorphisms rs17154774 of FRMD4A, rs77498336 ofGPR116, rs75949580 and rs187682251 of MAPK4.

WHY IMPORTANT?

These results highlight the potential for future genetic studies to evaluate the link between psoriasis and the metabolic syndrome.

POLLING QUESTION

Do you routinely screen your psoriasis patients for cardiovascular disease?

Association between IL-17 rs763780 and IL-17RA rs4819554 gene polymorphisms with response to biological drugs in psoriasis patients and beyond

Iulia-Ioana Morar, Alexandra Dana Pușcaș, Ștefan Cristian Vesa, Andreea Cătană, Cristian Pușcaș, Roxana Flavia Ilieș, Remus Ioan Orăsan

Abstract #1680

Poster ID P1923
e-Poster Hall, Wednesday 11 Oct

The IL-17 family of cytokines play a key role in the pathogenesis of psoriasis. The aim of this study was to determine if genetic single-nucleotide polymorphisms (SNPs) of IL-17F (rs763780) and IL-17RA (rs4819554) were associated with response to biological treatments and clinical characteristics.

The study included 81 patients with moderate-to-severe psoriasis who received biological treatments with anti-TNF, anti-IL23, anti-IL17 or anti-IL-12/23 agents.

The rs763780 polymorphism in the IL-17F gene was associated with response to infliximab and adalimumab when used as first-line biologic. There was no association with either SNP and second-line treatment response.

The rs4819554 polymorphism in the IL-17RA gene was associated with nail psoriasis and BMI.

WHY IMPORTANT?

Gene polymorphisms can help to predict treatment response.

POLLING QUESTION

What additional information is considered in the process of optimizing treatment for patients?

UBE2L3 reduces interleukin-1β secretion in epidermal keratinocytes and deficiency of UBE2L3 results in spontaneous psoriasis-like dermatitis

Xue-Yan Chen, Xiaoyong Man

Abstract #2233

Poster ID P2408
e-Poster Hall, Wednesday 11 Oct

The proinflammatory cytokine interleukin-1 beta (IL-1β) is an important mediator in psoriatic disease. Ubiquitin conjugating enzyme E2 L3 (UBE2L3) is thought to be an indirect regulator of IL-1β secretion by binding to ubiquitin ligases such as tripartite motif-containing protein 21 (TRIM21).

This project found UBE2L3 expression to be decreased in psoriatic epidermis, while IL-1β signalling was strongly activated. Stimulation of normal human epidermal keratinocytes with nigericin, adenosine triphosphate (ATP) and poly(dA:dT) caused downregulation of UBE2L3 and increased secretion of IL-1β. UBE2L3 overexpression reduced its binding with TRIM21, decreased STAT3 pathway activity and reduced levels of the IL-1β precursor pro-IL-1β. The reverse was seen when UBE2L was silenced.

Mice with epidermal deficiency of Ube2l3 developed spontaneous psoriasis-like skin disease. Overexpression of Ube2l3 ameliorated psoriasiform skin inflammation following imiquimod treatment with reduced pro-IL-1β and mature IL-1β levels in the epidermis.

WHY IMPORTANT?

UBE2L3 appears to have a protective role in the epidermis of psoriasis.

POLLING QUESTION

What other immune pathway do you consider under explored in psoriasis?

Type I/II immunity and cytotoxicity signature genes mark transcriptional programs of peripheral γδ T cells in untreated psoriasis vulgaris.

Stana Tokić, Maja Jirouš, Kristina Glavaš, Vera Plužarić, Marija Šola, Teuta Opačak Bernardi, Barbara Viljetić, Maja Tolušić Levak, Mario Štefanić

Abstract #2765

Poster ID P2452
e-Poster Hall, Wednesday 11 Oct

This study investigated the immunotranscriptome of peripheral blood CD3+γδTCR+ T cells in 12 people with psoriasis vulgaris (median PASI 7.4) and compared it to 11 matched controls.

Targeted RNA sequencing of 395 genes identified 36 differentially expressed genes including the Th1/2 lineage defining transcription factors STAT6 and TBX21. IRF1 (the master regulator of interferon/IFN signalling) and the IFNγ-inducible targets were overrepresented as well (ISG20, CD40, KLRK1, GPR18, IL2RB, q=2.1E-9, gene set enrichment analysis), together with the genes related to cytotoxicity (PRF1, GZMA, NKG7, SRGN, HLA-E, q=1.1E-9), cell trafficking (KLF2, CXCR4, GPR18, MIF, CORO1A, q=5.9E-11), and cell-cell adhesion (SELL, CD47, ITGAL, q=1.3E-7). Genes encoding members of the TCR signalosome (CD3D/E/G, ZAP70, CD247, q=1.7E-6) were also overexpressed, while the levels of IFI44L (a feedback regulator of IFN response), IL23A, and MTOR (which encodes the major nutrient-sensitive regulator of cell metabolism and stress response) were reduced.

WHY IMPORTANT?

Peripheral γδT cells in psoriasis show enhanced activation and cytotoxic capacity.

POLLING QUESTION

Can systemic treatment exert disease modifying effects in psoriasis?

Air pollutant and gut microbiota–derived metabolite – trimethylamine – is associated with systemic inflammation in psoriasis.

Mariusz Sikora

Abstract #5786

Poster ID P2066
e-Poster Hall, Wednesday 11 Oct

Gut bacteria-produced molecules and air pollution may be involved in the development and exacerbation of psoriasis. Plasma trimethylamine (TMA) is a gut bacteria metabolite of choline and carnitine. TMA is also an air pollutant and used in the production of plastics and disinfectants.

One hundred and twenty patients with mild to severe plaque psoriasis were included in the study.

There was a significant positive correlation between plasma TMA and inflammatory parameters. Older age, increased biomarkers of gut barrier integrity, decreased estimated glomerular filtration rate and presence of non-alcoholic fatty liver disease were associated with increased concentration of TMA in patients with psoriasis.

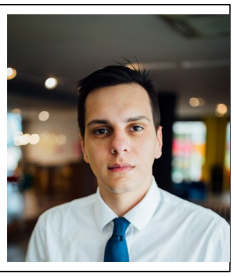
WHY IMPORTANT?

Comprehending the impacts of pollution and alterations in gut microbiota could contribute to the formulation of improved public health policies.

POLLING QUESTION

Can gut microbiota directed interventions treat psoriasis?

BASIC SCIENCE



- Dimitri Luz, MD, MsC, MBA
- Unisa and Hospital Israelita Albert Einstein
- Full GRAPPA member, Y-GRAPPA derm-rheum collab leader

Twitter: drdimitriluz
LinkedIn: Dimitri Luz

Immunological memory of psoriatic Lesions

Agnieszka Owczarczyk-Saczonek, Marta Kasprowicz-Furmańczyk, Joanna Czerwińska

Abstract #475

Poster ID P2324
e-Poster Hall, Wednesday 11 Oct

Tissue resident memory cells (TRM) are responsible for relapse of psoriasis in the same location as a previous lesion, with $CD8^+$ TRM in the epidermis and $CD4^+$ TRM in the dermis. A recent study found that treatment with guselkumab reduced the number of TRM and promoted Treg, while secukinumab had the opposite effect.

The authors of this abstract evaluated TRMs in psoriatic lesions prior to and after 12 weeks of therapy in patients treated systemically with methotrexate, secukinumab, ixekizumab or adalimumab. The most rapid response was observed after treatment with anti-IL-17 (at week 4). Treatment response was observed at week 12 with methotrexate and adalimumab.

A significant positive relationship was demonstrated between the expression of TRM markers in patients with plaque psoriasis and the duration of skin lesions.

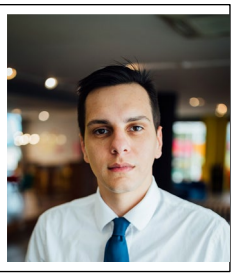
WHY IMPORTANT?

TRM explains the clinical phenomenon of psoriatic lesions relapsing in the same location.

POLLING QUESTION

Should we target TRM suppression on our treatments?

CLINICAL



- Dimitri Luz, MD, MsC, MBA
- Unisa and Hospital Israelita Albert Einstein
- Full GRAPPA member, Y-GRAPPA derm-rheum collab leader

Twitter: drdimitriluz
LinkedIn: Dimitri Luz

Prevalence of onychomycosis in psoriatic nails: a retrospective study of 157 cases

Hind Chagraoui, Hali Fouzia, Farida Marnissi, Soussi Maha, Soumia Chiheb

Abstract #4574

Poster ID P1705
e-Poster Hall, Wednesday 11 Oct

It is difficult to distinguish psoriatic nail disease from onychomycosis clinically. Moreover, fungal infection can be a reason for increased severity of psoriatic nail disease and treatment failure.

This study defined the prevalence of nail onychomycosis in 157 patients with psoriatic nail disease.

Mycological study showed a positive culture in 33.1% (52 cases), of which 59.6% (31 cases) were dermatophytes exclusively on the toenails. The most common species were Trichophyton Mentagrophyte variety Interdigitalis and Trichophyton Rubrum in toenails and Candidiasis Albicans in fingernails.

The prevalence of onychomycosis in this study lies between that reported in epidemiological studies which ranged between 15% and 79%.

WHY IMPORTANT?

Onychomycosis is common in patients with psoriatic nail disease.

POLLING QUESTION

Should we think on onychomycosis for every nail psoriasis patient?

Examining patterns and clusters of comorbidities in people with psoriasis

Alison Wrigh, Evangelos Kontopantelis, Richard Emsley, Charlotte Morris, Martin Rutter, Christopher Griffiths, Darren Ashcroft

Abstract #570

Poster ID P2329
e-Poster Hall, Wednesday 11 Oct

Primary care data from English general practices in the Clinical Practice Research Datalink identified 275,620 people diagnosed with psoriasis between 1998 and 2020.

Fifty-four percent of patients had at least one comorbidity present at diagnosis. Common comorbidities were anxiety and depression (17%), osteoarthritis (15%), asthma (9%), sleep disorders (8%), type 2 diabetes (6%), thyroid disorders (6%), cancer (5%), chronic obstructive pulmonary disease (4%), inflammatory arthritis (4%), inflammatory bowel disease (3%), gout (3%), renal disease (3%), diverticular disease (3%) and stroke (3%).

Latent class analysis identified five distinct comorbidity classes:

- 2.4% of patients in the “multiple comorbidities” class
- 15.9% in the “type 2 diabetes & renal disease” class
- 11.8% in the “sleep & mental health” class
- 1.8% in the “respiratory & osteoarthritis” class
- 68.2% in the “low comorbidity” class

WHY IMPORTANT?

Proposal of 5 main groups of comorbidities

POLLING QUESTION

Are we satisfactory screening our patients for comorbidities?

Establishing UK consensus to define a treat-to-target (T2T) outcome set that optimizes psoriatic patient wellbeing

Angelika Razzaque, Shareen Khan, Anthony Bewley, Chris Pitts, Sandy Mcbride, Angelika Razzaque, Shareen Khan, Anthony Bewley, Chris Pitts, Sandy Mcbride

Abstract #3510

Poster ID 2501
e-Poster Hall, Wednesday 11 Oct

The objective of this modified Delphi consensus project was to define a treat-to-target (T2T) outcome set that optimizes psoriatic patient wellbeing. This outcome set can then be used to complement future guideline development and patient care.

A panel of psoriasis experts developed 58 statements across six themes. Healthcare professionals across the UK were asked if they agreed with the statements. 180 responses were received and consensus (agreed at ≥75%) was achieved in 50/58 statements. The levels of agreement are shown in the figure below.

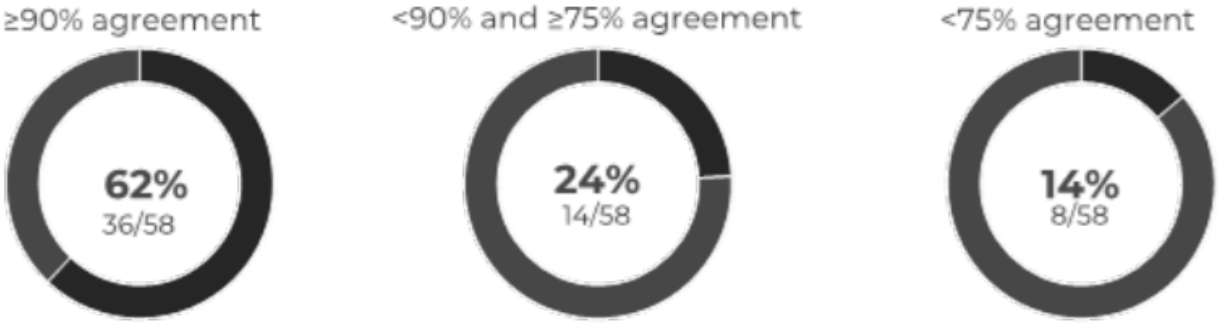
Implementation of these recommendations and measures across the care pathway in the UK has the potential to provide agreed psoriatic disease outcome targets that optimize psoriatic patient wellbeing, mitigate the potential variation of care, and complement future guideline development.

WHY IMPORTANT?

With the definition of a novel T2T, clinicians and patients can make shared decisions on the treatment goals they envisage, as a guidance for future treatment steps.

POLLING QUESTION

Do you practice *treat-to-target* with your patients?



Psoriasis and mental health comorbidities: A multinational analysis using the global healthcare study on psoriasis (GHSP)

Hannah Peterson, Edwin Korouri, Paige Kingston, Kathryn Lee, Margaret Huang, Danielle Yee, Rosario Agüero, Kevin Artiga, Fernando Valenzuela, Ricardo Romiti, Johannes Didaskalu, Alexander Egeberg, Hazel Oon, Julia-Tatjana Maul, April W. Armstrong

Abstract #1696

Poster ID P2378
e-Poster Hall, Wednesday 11 Oct

This study compared the prevalence of depression and anxiety in Brazil, Chile, China, Singapore, Switzerland, and the United States (US) as part of the Global Healthcare Study on Psoriasis.

2323 adults with psoriasis completed questionnaires including depression and anxiety queries.

Depression rates were: US 16.9%, Brazil 15.6%, Chile 13.9%, Switzerland 6.8%, Singapore 1.6%, China 0%. Multivariable analyses found that, compared to other countries, patients from the following countries were more likely to have depression: Brazil (aOR 1.66), Chile (aOR 1.52), and the US (aOR 1.21).

Anxiety rates were: US 12.4%, Switzerland 2.7%, Singapore 1.6%, Chile 0.2%, Brazil 0%, China 0%. Multivariable analyses found that, compared to other countries, patients from the following countries were more likely to have anxiety: US (aOR 12.01), Switzerland (aOR 2.88), and Singapore (aOR 1.14).

WHY IMPORTANT?

Psychiatric comorbidity prevalence varies worldwide, and cultural differences may reflect disclosure and approaches to these comorbidities.

POLLING QUESTION

Are you screening your patients for mental disorders?

The Evaluation of Serum Prolactin levels in Psoriasis

Madireddy Rakesh Reddy

Abstract #154

Poster ID 2314
e-Poster Hall, Wednesday 11 Oct

Prolactin has a proliferative effect on keratinocytes, epithelial cells, and lymphocytes. It also enhances T lymphocyte interferon production, promotes angiogenesis, and enhances secretion of chemokines such as CXCL9, CXCL10, CXCL11.

This study measured serum prolactin levels in 60 patients with psoriasis and 60 control participants in India. There was a male predominance with a male to female ratio of 2.53:1.

The mean serum prolactin levels in the cases and controls were 12.57+8.875 ng/ml and 6.71+2.684 ng/ml respectively. The serum prolactin levels were higher in females (17.57+12.54 ng/ml) than in males (10.59+6.01 ng/ml).

WHY IMPORTANT?

Discussion of new biomarkers and inflammation.

POLLING QUESTION

Will prolactin ever be used as psoriasis biomarker?

TREATMENT

- Arianna J Zhang, BA
- MD-MBA Candidate at Tufts School of Medicine
- Research Fellow at Brigham and Women's Hospital
- Grappa Early Career Member

Twitter: @AriannaZhang6
LinkedIn:
www.linkedin.com/in/ariannazhang13

Efficacy and safety of vunakizumab in moderate-to-severe chronic plaque psoriasis: a randomized, doubleblind, placebo-controlled phase 3 trial

Xu Jinhua, Kexiang Yan, Ling Han, Zhenghua Zhang, Fuqiu LI, Xiaodong Bi, Yuye LI, Litao Zhang, Xiaohua Wang, Linfeng LI, Jianyun Lu, Aie Xu, Sen Yang, Yan Lu, Jianfang Sun, Zhiming LI, Xiaohong Zhu, Meiying Jiang, Siping Zhang, Wenqing Wang, Yanling LI, Zudong Meng, Hongyi LI, Kuanhou Mou, Xiuping Han, Shanshan LI, Aijun Chen, Xin LI, Donghua Liu, Chunlei Zhang, Chao Ji, Yu Wang, Hao Cheng, Chunshui Yu, Zhiqiang Song, Chunjun Yang, Caixia Tu, Xianwei Cao, Danqi Deng, Tiechi Lei, Shoumin Zhang, Yanguo Zhang, Qingchun Diao, Yangfeng Ding, Wei LI, Xiaojing Cui, Xiaoyan Yao, Xiaoyan Bai, Fei Gu

Abstract #115

Poster ID 2311
e-Poster Hall, Wednesday 11 Oct

Vunakizumab is a humanized monoclonal IgG1/K antibody targeting IL-17A. In this abstract, the authors report results from a double-blinded, placebo-controlled phase 3 trial at 12 weeks and 52 weeks.

690 patients with moderate-to-severe chronic plaque psoriasis were randomly assigned to receive either vunakizumab induction (240 mg at weeks 0, 2, 4, and 8) or placebo. At week 12, those in the placebo arm were switched to active treatment. Vunakizumab was given every 4 weeks after induction.

At 12 weeks, the proportion of patients achieving PASI 90 were significantly higher with vunakizumab than with placebo (76.8% [95% CI 72.7-80.5] vs. 0.9% [95% CI 0.2-3.1], p<0.0001) and sPGA 0/1 (71.8% [95% CI 67.5-75.8] vs 0.4% [95% CI 0.1-2.4] p<0.0001). At 52 weeks, the PASI 90 and sPGA 0/1 response rates were sustained for the maintenance group.

The adverse events were reportedly mild and comparable between the vunakizumab and placebo (69.1% vs. 71.6%, respectively) groups.

WHY IMPORTANT?

Vunakizumab is an injectable therapy for psoriasis that demonstrates robust efficacy and a favourable safety profile at both 12 and 52 week time points.

POLLING QUESTION

Would you consider prescribing Vunakizumab over other IL-17A inhibitors?

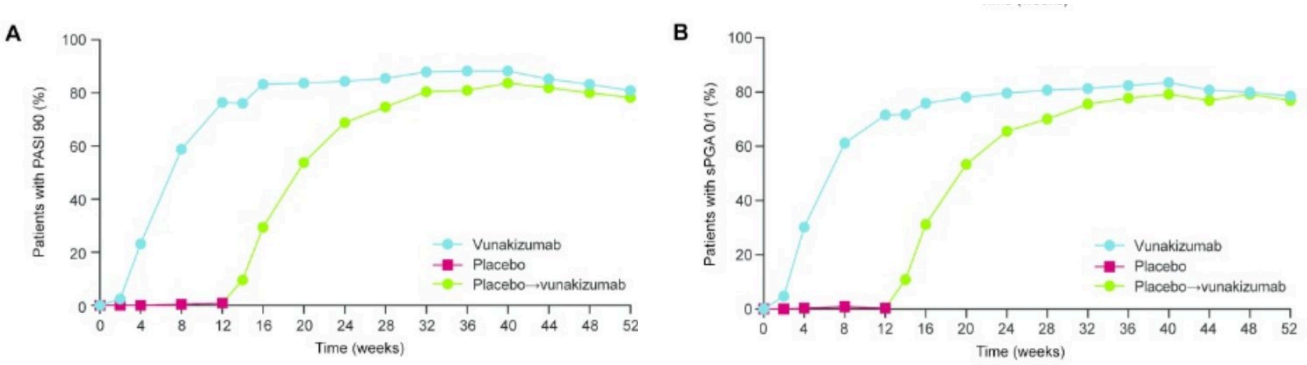


Figure 1. Proportion of patients achieving clinical response through to week 52 (intention-to-treat set). (A) PASI 90. (B) sPGA 0/1. Missing data were imputed as non-responses.

Response to IL-17A inhibitors according to prior biologic exposures: a Danish nationwide study

Nikolai Loft , Alexander Egeberg, Daniel Isufi, Mads Kirchheiner Rasmussen, Lars Erik Bryld, Tomas Norman Dam, Kawa Khaled Ajgeiy, Trine Bertelsen, Lone Skov

Abstract #396

Poster ID P2320
e-Poster Hall, Wednesday 11 Oct

This abstract sought to explore whether previous exposure to an IL-17 inhibitor affects treatment response to subsequent treatment with another IL-17 inhibitor.

The authors compared the proportion of patients achieving PASI≤2 when treated with an IL-17A inhibitor (secukinumab or ixekizumab) in those with prior exposure to an IL-17A inhibitor vs. those with prior exposure to a biologic other than an IL-17A inhibitor. Data from the Danish patient registry DERMBIO were analysed.

Chi-square analysis showed no difference in the proportion of patients achieving PASI≤2 between the two groups after 3 months (54% vs. 57%, p = 0.59; n = 514), 6 months (70% vs. 66% p = 0.42; n=465), and 12 months (69% vs. 60%, p=0.14; n=397).

Patients with prior treatment discontinuation of IL-17A inhibitors were further subdivided into those discontinued due to treatment failure and those discontinued due to reasons other than treatment failure. Again, no differences in the proportion of patients achieving PASI ≤2 after 3 months (54% vs. 55%, p = 0.95), 6 months (71% vs. 71%, p=-0.96), and 12 months (69% vs. 69%, p=0.97) were observed between these two categories.

WHY IMPORTANT?

Prior exposure to and treatment failure on an IL-17A inhibitor does not affect response rates to subsequent therapy with another IL-17A inhibitor.

POLLING QUESTION

In a patient that has failed an IL17 inhibitor, would you try another 17A inhibitor or switch to a biologic with a different cytokine target?

Effects of apremilast on quality of life and skin clearance in men and women with genital psoriasis: Subgroup analysis from the phase 3 DISCREET study

Joseph Merola, Lawrence C. Parish, Lyn Guenther, Charles Lynde, Jean-Philippe Lacour, Petra Staubach-Renz, Sue Cheng, Maria Paris, Cynthia Deignan, Shauna Jardon, Mindy Chen, Kim A. Papp

Abstract #1259

Presentation ID FC08.4
Room M1+2
Friday 13 Oct 16.30-16.40 BST

Genital psoriasis affects up to 63% of the psoriatic population at some point in the course of their disease. It is highly stigmatizing, often overlooked, and undertreated. In a post-hoc analysis, the authors report male and female subgroup findings from DISCREET, a phase 3 clinical trial evaluating the efficacy of apremilast (APR) to treat genital psoriasis.

Using a randomized, placebo-controlled double-blind study design, patients were assigned 1:1 to APR 30 mg BID or matching placebo for 16 weeks. The two key endpoints were change from baseline DLQI question 9 (sexual difficulties), and achievement of sPGA-G response of 0 (clear) or 1 (almost clear) with a ≥2 point reduction from baseline.

At 16 weeks, there was a treatment difference favouring APR compared to placebo, with a least square mean change from DLQI baseline question 9 score of 0.27 (95% CI: -0.52, -0.02) in men and 0.41 (95% CI: -0.082, 0.01) in women. The group treated with APR had a greater change from baseline total DLQI (-2.62 [95% CI: -4.49, -0.76] for men; -2.78 [95% CI: -5.66, 0.10] for women) and modified sPGA-G response compared to placebo at week 16. 35.7% of men treated with APR achieved sPGA-G response compared to 18.6% of men receiving placebo. 48.7% of women receiving APR achieved sPGA-G response compared to 21.6% of those receiving placebo.

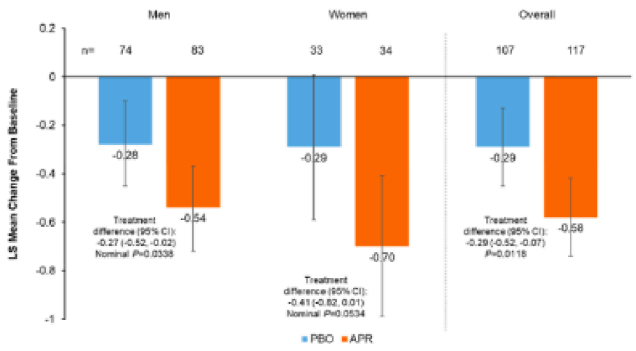
WHY IMPORTANT?

Apremilast is the first systemic treatment studied for genital psoriasis. It demonstrated improved sexual health and QoL in patients with genital psoriasis.

POLLING QUESTION

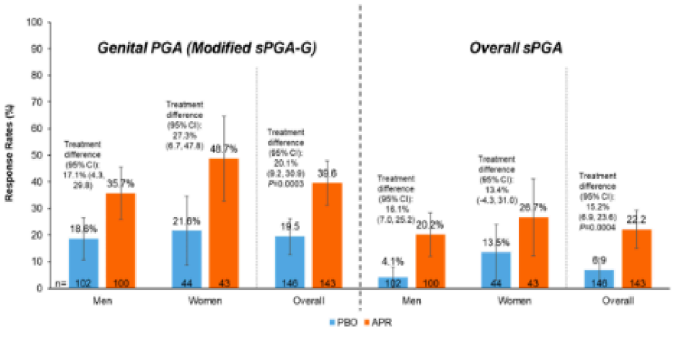
How often do you inquire about sexual difficulties relating to psoriasis?

Figure 1. Change From Baseline in DLQI-Q9 (Sexual Difficulties) at Week 16



Intent-to-treat population.
Error bars represent 95% CI.
Mixed-effect model for repeated measures used for missing values.
DLQI-Q9 asks, "Over the last week, how much has your skin caused any sexual difficulties?" It is scored on a scale from 0 (not relevant or not at all) to 3 (very much).
APR=apremilast; CI=confidence interval; DLQI=Dermatology Life Quality Index; LS=least squares; PBO=placebo.

Figure 3. Modified sPGA-G and Overall sPGA Response at Week 16



Intent-to-treat population.
Error bars represent 95% CI.
Multiple imputation used for missing values.
Modified sPGA-G response defined as a score of 0 (clear) or 1 (almost clear) with ≥2-point reduction from baseline.
sPGA response defined as a score of 0 (clear) or 1 (almost clear) with ≥2-point reduction from baseline.
APR=apremilast; CI=confidence interval; sPGA=static Physicians Global Assessment; sPGA-G=static Physician Global Assessment of Genitalia; LS=least squares; PBO=placebo.

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Join us for the next in our series of GRAPPA Virtual Congress Highlights, where we will be highlighting the hottest topics from the EADV 2023 Congress in Berlin. This event is open to all so tell your colleagues and help spread the word.

Click here to register.