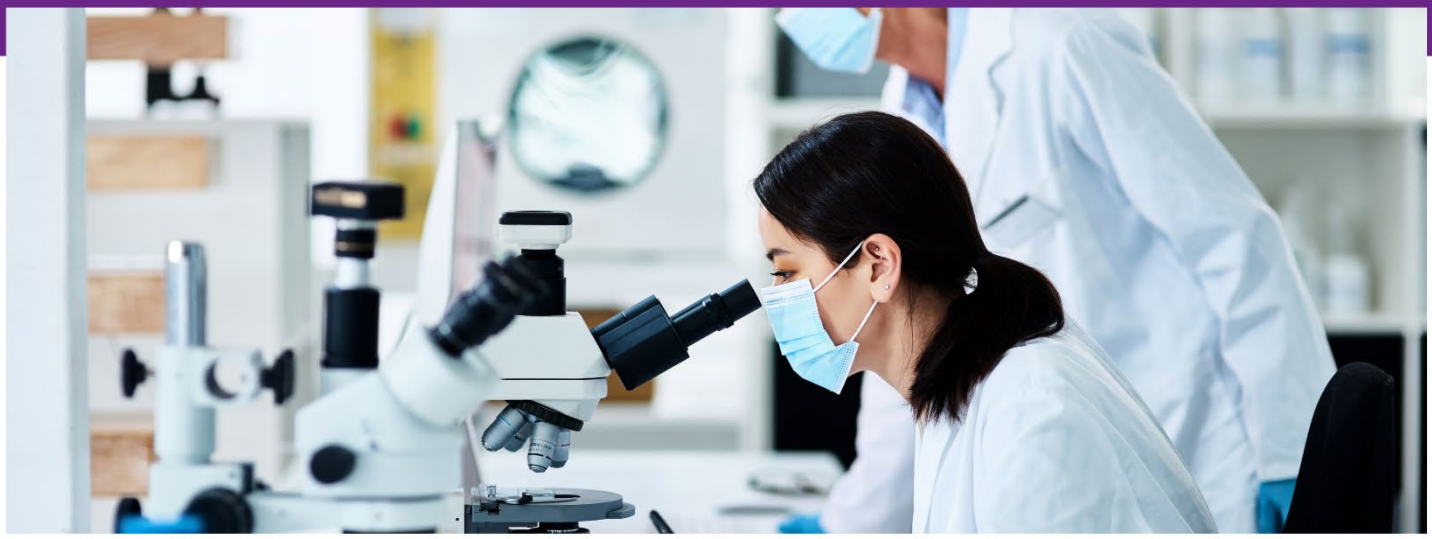
ACR 2023

DO NOT MISS HIGHLIGHTS IN PSORIATIC DISEASE

NOVEMBER 2023



Y-GRAPPA members prepared this Newsletter. It highlights some of the very interesting abstracts on psoriatic disease that will be presented at the 2023 ACR Congress in San Diego.

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NEWSLETTER

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YOUNG GROUP FOR RESEARCH AND ASSESSMENT OF PSORIASIS AND PSORIATIC ARTHRITIS

BASIC SCIENCE

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- Attending physician, Department of Rheumatology, University Hospital Zurich & Swiss Ultrasound Center Basel, Switzerland
- Research focus: Role of synovial fibroblast in PsA, Comorbidities in PsA, Ultrasound

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Synovial Shaping of Skin-derived Migrating Immune Cells Determines Initiation of Inflammation in Psoriatic Arthritis

Maria Gabriella Raimondo

Abstract Session
Tuesday, November 14th
2:00PM-3:30PM

Abstract #2440

https://acrabstracts.org/abstract/synovial-shaping-of-skin-derived-migrating-immune-cells-determines-initiation-of-inflammation-in-psoriatic-arthritis/

Approximately 30% of patients with psoriasis develop psoriatic arthritis (PsA). The mechanisms driving this transition remain elusive. This study investigated cellular trafficking from inflamed skin to joints by utilizing a pre-clinical mouse model with IL-23 overexpression.

All mice developed cutaneous lesions, but joint inflammation was discerned solely in those with certain genetic markers. However, immune cell migration from psoriatic skin to the joints was observed in both arthritic and non-arthritic mice. A specific monocyte subset (CD2+ MCHII+ monocytes) consistently migrated from skin to synovial tissues.

Within the joint milieu, these monocytes diverged into two differentiation pathways: one inducing inflammation, similar to PsA, and the other remaining non-inflammatory. Crucially, interactions with specific synovial stromal cells (sublining synovial fibroblasts) appeared to dictate this differentiation trajectory. Human biopsy analyses mirrored these findings.

In essence, skin-derived monocytes play a key role in PsA pathogenesis, with their inflammatory potential modulated by synovial interactions. These findings have mechanistic and diagnostic implications.

WHY IMPORTANT?

This study illuminates the cellular pathways transitioning psoriasis to PsA, paving the way for future treatments.

POLLING QUESTION

Do you think by changing the synovial milieu (e.g. by inhibiting certain synovial fibroblasts) the transition from psoriasis to PsA could be inhibited?

Upregulation of RANKL in the Skin of Patients with Psoriatic Arthritis

Maria de la Luz Garcia-Hernandez

Abstract Session
Tuesday, November 14th
2:00PM-3:30PM

Abstract #2441

https://acrabstracts.org/abstract/upregulation-of-rankl-in-the-skin-of-patients-with-psoriatic-arthritis/

This study delved into the roles of the proteins RANKL (Receptor Activator of Nuclear Factor kB Ligand) and DC-STAMP (Dendritic Cell-Transmembrane Protein) in PsA pathogenesis. It specifically examined whether their expression in the skin of patients with psoriasis with and without inflammatory joint involvement might spur monocyte differentiation into osteoclast precursors (OCPs).

Through a series of skin biopsies and advanced analyses, it was revealed that RANKL expression was higher in PsA skin as compared to patients without joint involvement. They also found an increased number of dermal DC-STAMP+CD14+ OCP in the dermis of PsA skin plaques. Moreover, a combination of TNF and IL1-7 significantly induced RANKL expression in keratinocytes.

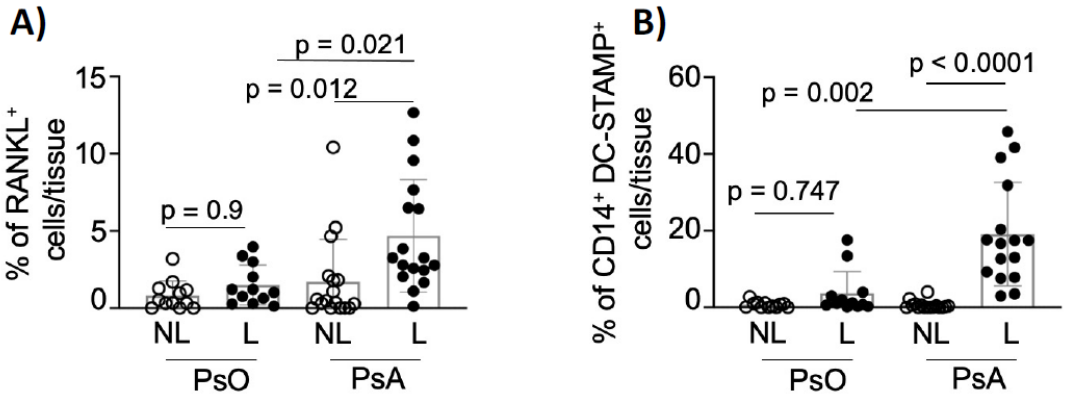
This heightened expression and the presence of certain cell types in PsA skin underscore a potential mechanism which drives the progression of disease, from psoriasis without inflammatory joint involvement to PsA.

WHY IMPORTANT?

The study identifies distinct cellular and protein expressions in PsA skin, elucidating potential mechanisms differentiating PsA from psoriasis and informing future therapeutic strategies.

POLLING QUESTION

What do you think about using RANKL in psoriasis plaques as a potential predictive or diagnostic biomarker?



Graphs show mean ± standard of 12 Psoriasis (PsO) and 16 Psoriatic-Arthritis (PsA) lesional (L) and non-lesional (NL) skin biopsies.
A) The morphometric analysis shows higher percentage of RANKL+ and **B)** higher percentage of DC-STAMP+ CD14+ cells (OCP) in PsA skin biopsies. Graphs show mean ± standard of 12 PsO and 16 PsA lesional and non-lesional skin biopsies.

Multi-Omics Analyses Identify Metabolic Pathways That Differentiate Psoriatic Arthritis from Psoriasis

Vinod Chandran

Poster Session C
Tuesday, November 14th
9:00AM-11:00AM

Abstract #1795

https://acrabstracts.org/abstract/multi-omics-analyses-identify-metabolic-pathways-that-differentiate-psoriatic-arthritis-from-psoriasis/

Distinguishing PsA from psoriasis without PsA (PsO) can be challenging in certain cases (e.g. early disease, patients with overlapping erosive osteoarthritis or fibromyalgia), largely because of the absence of clear diagnostic markers.

To address this, an integrated multiomics study was conducted, examining DNA, RNA, miRNA, and metabolites from samples from 102 patients with PsA and 100 with PsO.

Using a sophisticated random forest model, 200 biomarkers, including 97 metabolites, 77 miRNAs and 26 mRNAs, were found to discriminate between PsA and PsO. Nine of the miRNAs target six of the mRNAs and were analysed further (see Figure below).

A remarkable finding was different enrichments in phospho- and glycerophospholipid metabolic pathways.

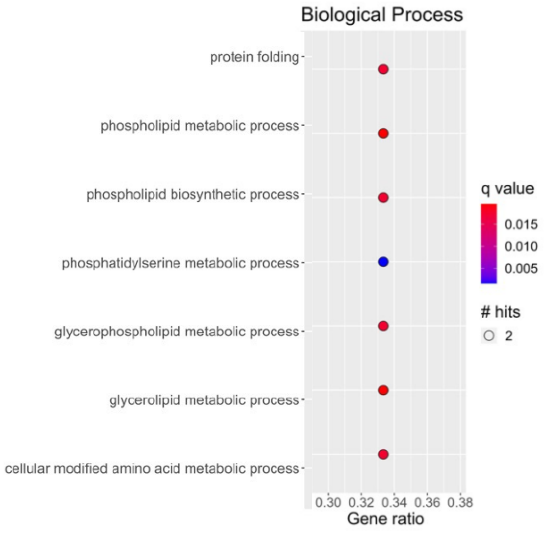
The study provides a comprehensive insight into molecular differences between PsA and PsO. It underlines the possible importance of phospholipidic pathways in the evolution of psoriatic conditions.

WHY IMPORTANT?

The discovery of specific biomarkers provides a promising avenue to accurately distinguish between PsA and PsO, paving the way for enhanced diagnostic precision.

POLLING QUESTION

Could integrated multiomics be the key to distinguishing PsA from PsO?



Gene Ontology enrichment analysis results for the 6 genes from the 200 biomarkers identified as targets of 9 miRNAs from the same 200 biomarkers. Variations in phospholipid profiles between PsA and PsO have been previously observed, suggesting a potential connection with the immune system.

BASIC SCIENCE

- Vinod Kumar, PhD
- Assistant Professor, PGIMER, Chandigarh, India
- Y-GRAPPA member,
- PsA, Stem Cell therapy, Genetics, and RA

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Identifying Differentially Expressed Genes to Predict TNF-Alpha and IL-17A Inhibitor Response in Psoriatic Arthritis

Quan Li

Poster Session C
Tuesday, November 14th
9:00AM-11:00AM

Abstract #2235

https://acrabstracts.org/abstract/identifying-differentially-expressed-genes-to-predict-tnf-alpha-and-il-17a-inhibitor-response-in-psoriatic-arthritis/

Biological therapies that target immune system pathways have been a major advancement in treating moderate to severe PsA. However, 30-40% of patients do not respond to biologics.

This study aimed to determine if CD8 T-cell transcriptomic data obtained at baseline could predict response to TNFi and IL-17Ai using PCA analysis discriminated responders vs. non-responder.

Twenty-one patients with PsA received TNFi, and 61% responded (Figure A). Before treatment transcriptomic data identified INFLAMMATORY_RESPONSE, INTERFERON_GAMMA_RESPONSE and IL6_JAK_STAT3_SIGNALING as the top upregulated pathways and *PM20D1, CLIC6, OR1L8, KLHL12, GPALPP1* as the most differentially expressed genes.

Of 28 patients with PsA (n=28) treated with IL-17i, 40% responded (Figure B). Pathways like MITOTIC_SPINDLE, E2F, G2M were identified as the top down-regulated pathways after IL-17i treatment response and *C19orf81, NMI, RPIA, ALG1L, TUBA3E* as differentially expressed genes.

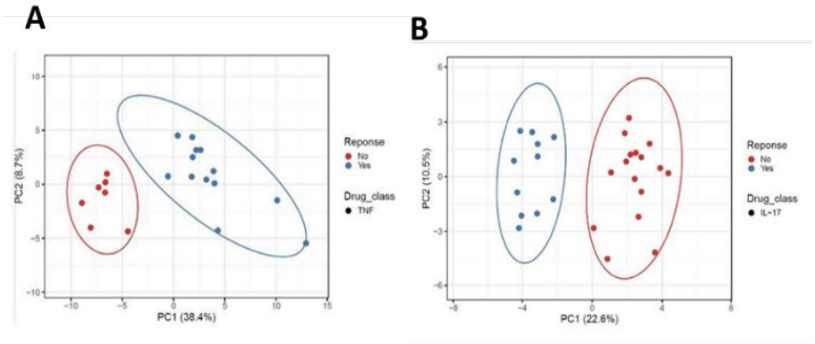
In summary, the study suggests that gene expression patterns vary among PsA patients, and further research is needed to explore these findings

WHY IMPORTANT?

Transcriptomic heterogeneity may predict treatment outcomes & potentially allow for more personalized treatment decisions in the future.

POLLING QUESTION

Is it cost-effective to screen all the patients before treatment?



Pharmacological Inhibition of PRMT5 Demonstrates Broad Efficacy in Multiple Preclinical Models of Autoimmunity and Inflammation by Suppressing Th1, Th17 and TNF-Mediated Inflammatory Responses

Neha Bhagwat

Poster Session A
Sunday, November 12th
9:00AM-11:00AM

Abstract #0080

https://acrabstracts.org/abstract/pharmacological-inhibition-of-prmt5-demonstrates-broad-efficacy-in-multiple-preclinical-models-of-autoimmunity-and-inflammation-by-suppressing-th1-th17-and-tnf-mediated-inflammatory-responses/

PRMT5 (Protein arginine methyltransferase 5), a protein modifier, promote inflammatory T-cell responses, particularly those driven by Th1 and Th17 cells. Thus, selective PRMT5 inhibitors (PRMT5i) offer a novel treatment for T-cell-mediated autoimmune and inflammatory disorders.

This study tested this immunomodulatory effect of PRMT5i in vitro (using human Th1 & Th17 cells) as well as in *in vivo* using various autoimmune disease rodent models: SLE (MRL/lpr), Psoriasis (IMQ-induced), RA (CIA-mouse model), EAN (rat model), & GCA (human artery/NSG mouse chimera).

Results showed that PRMT5i improved disease severity in all the tested disease models. This included reduction in proteinuria, PASI score (Figure A), blood vessel infiltration of immune cells & CIA Score (Figure C). PRMT5 inhibition was also able to inhibit T cell proliferation and differentiation of Th1 and Th17 cells. There was an increase in Treg cell numbers and decrease in inflammatory cytokines like RNF, IFNy, IL-21, BAFF, IL-17A, IL-22 (Figure B).

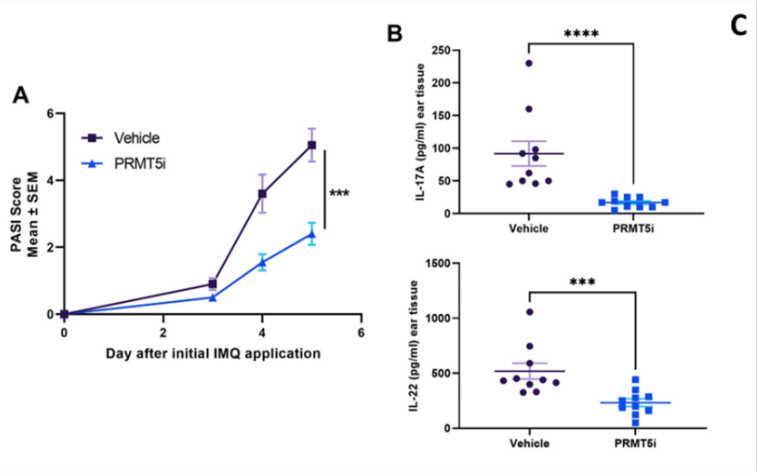
According to these findings, PRMT5i has therapeutic potential for inflammatory and autoimmune diseases.

WHY IMPORTANT?

The protein function modifier PRMT5 has therapeutic potential for inflammatory and autoimmune diseases.

POLLING QUESTION

Is the effect of PRMT5 inhibition specific towards pathogenic cells or can it equally target other cells too?



Deep Cellular Immune Profiling in Psoriatic Arthritis Correlates with Imaging Phenotypes and Response to Targeted Advanced Therapy

Lihi Eder

Abstract Session
Monday, November 13th
4:00PM-5:30PM

Abstract #1689

https://acrabstracts.org/abstract/deep-cellular-immune-profiling-in-psoriatic-arthritis-correlates-with-imaging-phenotypes-and-response-to-targeted-advanced-therapy/

This study addressed the question: Does peripheral blood immune cell profiles relate to baseline clinical, imaging features and treatment response in patients with PsA?

40 patients with PsA treated with IL17i (n=21), TNFi (n=16) & JAKi (n=3) were included and 60% achieved an ACR20 response. Three $CD3^+$ immune cell clusters were studied and had different associations (Figure 1B, 1C):

Cluster 1 (γδT cells and $CD8^+$ naïve cells): associated with lower sonographic inflammation.

Cluster 2 (Central Memory (CM) and Effector Memory (EM) $CD4^+$ T cells): associated with a) higher sonographic inflammation, b) lower ACR20 response, c) higher DAPSA.

Cluster 3 (CD4+ and CD8+ Terminal Effector (TE) T cells and Th1 cells): Associated with high peritednon inflammation.

Cell type analysis revealed: decrease in DAPSA score with increase in $CD8^+$ cells, high γδT cells have increased chances of ACR20 response & high EM, CM and Th1 cells have lowest response (Table 1). Compared to γδT cells and $CD8^+$ naïve cells, $CD4^+$ memory and Th1 cells were linked to severe synovitis and enthesitis and poor response to advanced therapies.

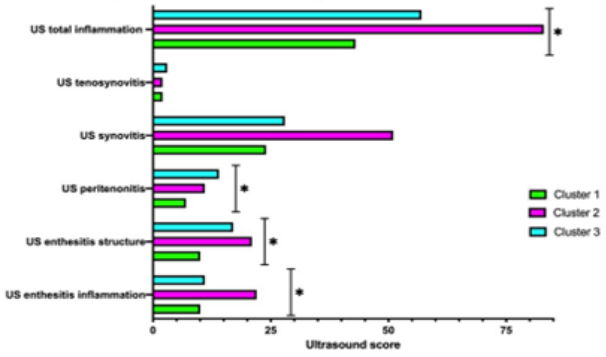
WHY IMPORTANT?

Different immune cell clusters can predict the response rates in PsA patients.

POLLING QUESTION

Which strategy—using single-cell types or cell clusters—offers a more precise way to forecast the onset, progression, & treatment response in PsA patients?

1B. Sonographic features by immune cluster



1C. Clinical features by immune cluster

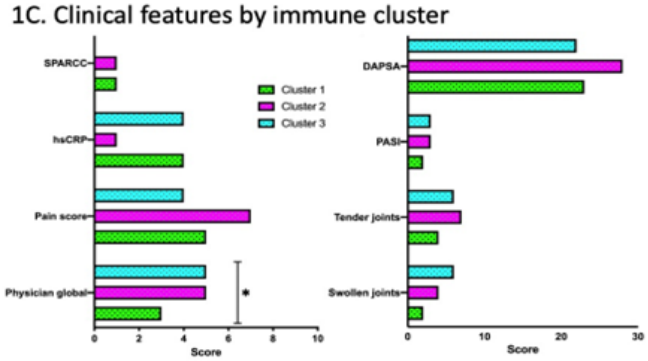
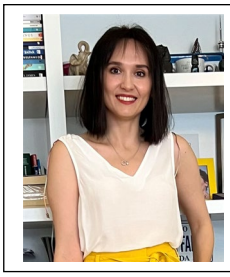


Table 1: The association between baseline immune profile* and clinical response to targeted advanced therapies at 3 months - GEE regression model (N=40)

	ACR20 response (24 events)		DAPSA change**	
Immune cell population	**Odds Ratio (95% CI)**	**P value**	**β coefficient (95% CI)**	**P value**
Cluster 2 vs. Cluster 1	**0.15 (0.02, 0.93)**	**0.04**	**12.28 (5.69, 18.86)**	**<0.001**
Cluster 2 vs. Cluster 3	**0.09 (0.01, 0.68)**	**0.02**	**13.85 (7.73, 19.97)**	**<0.001**
CD8+ T cells	6.85 (0.65, 71.62)	0.10	**-13.2 (-20.6, -5.7)**	**<0.001**
CD8+ naïve T cells	1.43 (0.52, 3.92)	0.47	**-5.07 (-9.73, -0.40)**	**0.03**
CD8+ CM T cells	0.72 (0.25, 2.09)	0.54	-0.20 (-6.80, 6.40)	0.95
CD8+ EM T cells	2.98 (0.58, 15.41)	0.18	-2.52 (-18.52, 13.48)	0.75
CD8+ TE T cells	1.68 (0.77, 3.67)	0.18	-4.18 (-8.60, 0.25)	0.06
CD4+ T cells	0.002 (0.000, 2.40)	0.08	**31.05 (13.47, 48.64)**	**<0.001**
CD4+ Naïve T cells	**0.23 (0.05, 0.97)**	**0.04**	**11.64 (3.36, 19.93)**	**0.004**
CD4+ CM T cells	0.38 (0.03, 4.35)	0.42	**15.60 (5.79, 25.42)**	**0.001**
CD4+ EM T cells	0.14 (0.02, 1.29)	0.07	**12.01 (4.62, 19.39)**	**0.001**
CD4+ TE T cells	1.47 (0.51, 4.24)	0.46	1.30 (-6.88, 9.49)	0.99
γδ T cells	**2.92 (1.02, 8.35)**	**0.04**	1.30 (-6.88, 9.49)	0.75
MAIT NKT cells	1.98 (0.97, 4.06)	0.05	-2.47 (-5.00, 0.06)	0.047
Regulatory T cells	0.90 (0.20, 4.14)	0.89	6.25 (-0.42, 12.92)	0.06
Th1 cells	**0.20 (0.04, 0.86)**	**0.03**	14.20 (-7.19, 35.58)	0.18
Th2 cells	1.31 (0.30, 5.82)	0.71	8.51 (-38.04, 55.06)	0.71
Th17 cells	1.73 (0.43, 6.86)	0.42	1.83 (-5.32, 8.97)	0.60

*cell count/CD3+ cells; **difference in baseline-follow up DAPSA score adjusted for DAPSA score at baseline; CM- central memory; DAPSA – disease activity in psoriatic arthritis; EM – effector memory; MAIT NKT – mucosal associated T and Natural Killer T; TE-terminal effector; Th – T helper

BASIC SCIENCE



- Tugba Izci Duran, Assoc. Prof.
- MD, Denizli State Hospital
- Y-GRAPPA member, participates in the Newsletter Committee
- Research focus: Spondyloarthritis such as PsA and AxSpA

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Exploring the Mechanism of Anti-TNFα Therapy Non-response in Psoriatic Arthritis: The Role of TNF Receptor 2 Polymorphisms rs1061622

James Sullivan

Poster Session C
Tuesday, November 14th
9:00AM-11:00AM

Abstract #1791

https://acrabstracts.org/abstract/exploring-the-mechanism-of-anti-tnf%ce%b1-therapy-non-response-in-psoriatic-arthritis-the-role-of-tnf-receptor-2-polymorphisms-rs1061622/

Rs1061622 polymorphisms in the TNFα receptor 2 (TNFR2) gene have been associated with treatment response in PsA. This study investigated the signalling differences between TNFR2 polymorphisms resulting in a T allele (TNFR2-196M) and G allele (TNFR2-196R).

Treatment with a TNF inhibitor did not affect basal ICAM-1 (a TNFR2-dependent proinflammatory gene) expression in cell cultures. Human umbilical vein endothelial cells (HUVEC) with overexpression of TNFR2-196R showed increased ICAM-1 and IL-1β mRNA levels, while those with TNFR2-196M did not. In addition, HUVEC with the G-allele had higher basal expression of proinflammatory genes (IL-1β, IL-6, ICAM-1, GM-CSF2, CXCL2, E-selectin, Il-8) in the absence of TNFα (Figure 3) than those with the T-allele.

At least one G allele for TNFR-196R confers a proinflammatory activity that is independent of TNFα. This could point towards the mechanism underlying the association between response to TNFi and rs1061622 polymorphisms.

WHY IMPORTANT?

Gene polymorphisms can help to predict treatment response.

POLLING QUESTION

How would this data help you in the path towards precision medicine?

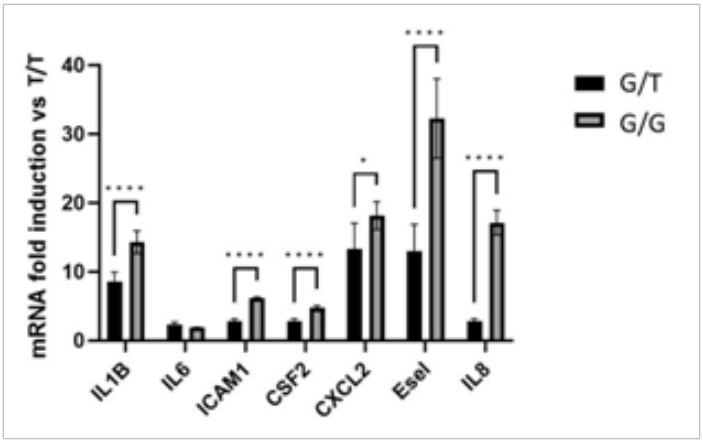


Figure 3. TNFα independent constitutive inflammatory activity in HUVEC expressing at least one G allele. Total RNA was extracted from HUVEC with T/T, T/G, or G/G genotypes. mRNA levels of indicated genes were quantified using RTqPCR after normalizing with mRNA levels of RPL_32, a housekeeping gene not induced by cytokines, including TNFα.

Regulatory Role of JAK-1/TYK2 Signaling on the Pannus Formation: Novel Mechanisms for JAK Inhibitors in Psoriatic Disease

Siba Raychaudhuri

Poster Session C
Tuesday, November 14th
9:00AM-11:00AM

Abstract #1787

https://acrabstracts.org/abstract/regulatory-role-of-jak-1-tyk2-signaling-on-the-pannus-formation-novel-mechanisms-for-jak-inhibitors-in-psoriatic-disease/

This abstract hypothesized that JAK/STAT signalling induced by IL-9/22 plays a role in regulating the proliferative cascades of synovial cells (FLS) in PsA.

FLS from 10 subjects with PsA were cultured with rIL-9 and rIL-22. Immunoblot studies were performed to evaluate JAK1/pJAK1, TYK2/pTYK2, STAT1/pSTAT1, STAT3/pSTAT3 in the presence or absence of specific JAK inhibitors.

In cultured FLS, rIL-22 and rIL-9 led to an increase in phosphorylation of JAK1/TYK2 and JAK1/JAK3 respectively compared to culture media only ($p< 0.01$). rIL9/rIL22 also phosphorylated STAT3/RORγt. Other observations were that FLS proliferation, IL-6, IL-8 and MMP-3 production were induced by rIL-22 and rIL-9 and regulated by JAK1/TYK2 and JAK-1,3 respectively. JAK inhibitors blocked these effects ($p< 0.01$).

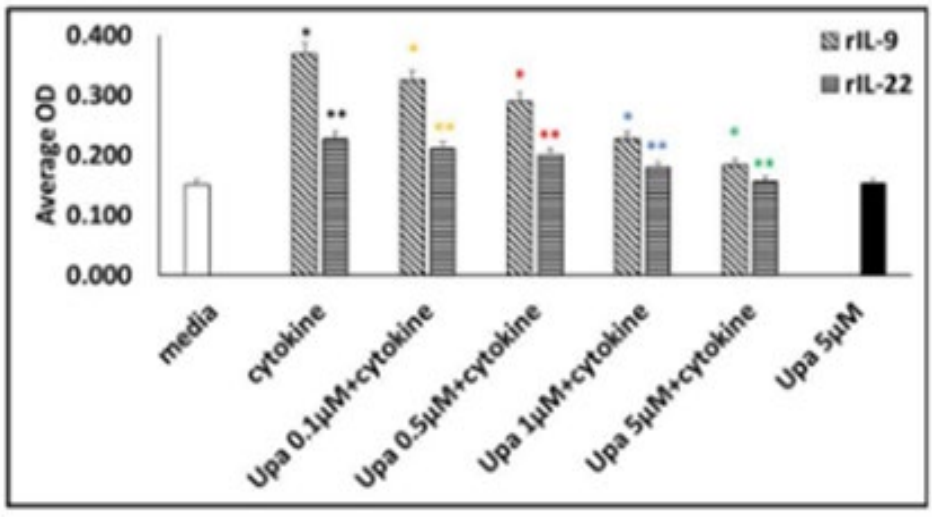
WHY IMPORTANT?

It provides new insight into the role of JAK1 and TYK2 signalling on FLS proliferation, and FLS as targets of PsA treatments.

POLLING QUESTION

How do these mechanisms impact the safety of JAK inhibitors?

Figure 1: JAK_1 regulates rIL-9/rIL_22 induced proliferation of FLS



Role of GITR/GITRL Interaction in Modulating T Helper 9, T Helper 17 and T Regulatory Response in Psoriatic Arthritis

Chiara Rizzo

Poster Session C
Tuesday, November 14th
9:00AM-11:00AM

Abstract #1778

https://acrabstracts.org/abstract/role-of-gitr-gitrl-interaction-in-modulating-t-helper-9-t-helper-17-and-t-regulatory-response-in-psoriatic-arthritis/

The IL-23/IL-17 axis and IL-9 overexpression play major roles in PsA pathogenesis. There is a correlation between IL-9 and Glucocorticoid-induced Tumour Necrosis Factor-related receptor (GITR). The GITR ligand (GITRL) is expressed on antigen presenting cells. Considering the pro-inflammatory function of GITR, the authors of this abstract evaluated the effects of GITR/GITRL interactions in PsA.

Peripheral blood mononuclear cells from 80 patients with PsA and 10 healthy controls were studied.

There was upregulation of GITRL on monocytes (CD14+), dendritic cells (CD11c+) and B cells (CD19+) in patients with PsA, but no cell frequency differences were detected. After stimulation with anti-CD3-CD28, Th9 and Th17 expansion was observed ($p< 0.05$); and this increased further in the presence of recombinant GITR agonist ($p< 0.05$, Figure 1).

This study supports a potential role of the GITR/GITRL axis in PsA.

WHY IMPORTANT?

These results highlight a new pathway that might be explored as a target in PsA.

POLLING QUESTION

What side effects would be expected from targeting the GITR/GITRL axis?

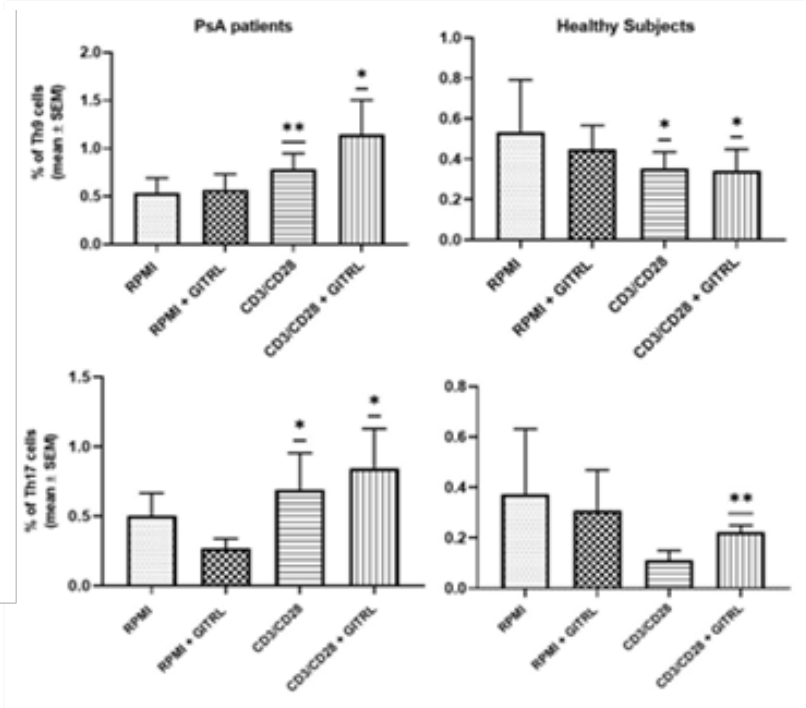


Figure 1. Recombinant GITRL effect on Th9 and Th17 frequency.
*Frequency of Th9 and Th17 analysed in four different conditions: RPMI, RPMI + GITRL, CD28/CD28 activation beads, CD3/CD28 + GITRL in PsA patients (left panel of the figure) and in healthy controls (right panel of the figure), respectively. *p<0.05*

CLINICAL

- Pamela Diaz, MD
- Clinical Assistant Professor, Pontificia Universidad Catolica de Chile
- Young GRAPPA member. Participates in the education committee and Slide Library
- Research focus: psoriatic arthritis, spondylarthritis

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Higher Levels of High-sensitivity CRP Are Associated with Future Risk of Developing Psoriatic Arthritis Among Patients with Psoriasis: A Prospective Cohort Study

Lihi Eder

Poster Session A
Sunday, November 12th
9:00AM-11:00AM

Abstract #0484

https://acrabstracts.org/abstract/higher-levels-of-high-sensitivity-crp-are-associated-with-future-risk-of-developing-psoriatic-arthritis-among-patients-with-psoriasis-a-prospective-cohort-study/

High-sensitivity C-reactive protein CPR (hs-CRP) is a biomarker of systemic inflammation. This study investigated hs-CRP as a prognostic factor for developing PsA in patients with psoriasis.

Data were obtained from a prospective cohort of patients with psoriasis without PsA. Clinical assessment by a rheumatologist was done at baseline and annually. Hs-CPR levels were measured at baseline.

Among 589 patients with psoriasis (mean follow-up of 7.5 years), 57 developed PsA during the follow-up period (1.2 events/year). Mean hs-CRP levels were 3.1±5.5 mg/dL, and the level was significantly higher in patients with arthralgia, obesity, and females.

Higher hs-CRP levels at baseline were associated with an increased risk of developing PsA in univariate analysis (HR 1.03, 95%CI [1.01-1.05], p=0.002) (Figure). This association persisted after adjusting for other known risk factors for PsA (HR 1.03, 95%CI 1.02,105, p=0.002).

WHY IMPORTANT?

In patients with psoriasis, higher levels hs-CRP were associated with an increased risk of PsA.

POLLING QUESTION

Does hs-CPR help to identify patients with psoriasis who need closer follow-up for the development of PsA?

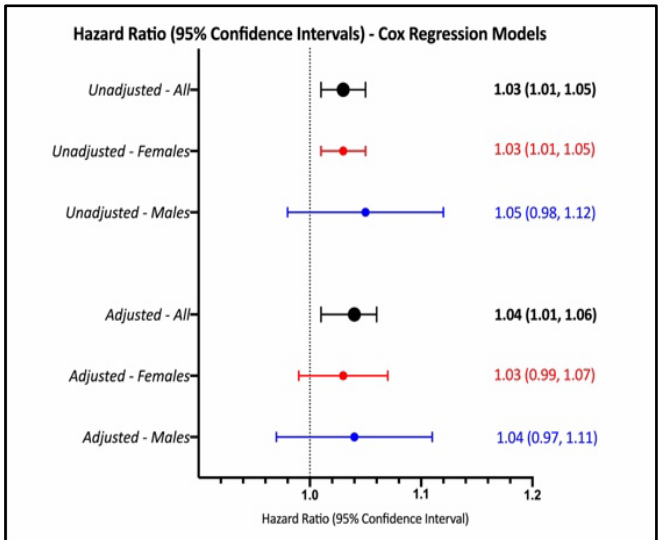


Figure 1: The association between hsCRP and development of PsA by Cox proportional hazards models. Univariate and multivariable regression models adjusted for age, sex, psoriasis duration, PASI, nail lesions, BMI, pain, FACIT-fatigue, use of biologics, and use of non-biologic systemic therapy/UV therapy

Spinal Inflammation a Dominant Pathology in Psoriatic Arthritis: Characterization and Quantification by In-Vivo 18F-FDG Total-Body PET/CT Imaging

Siba Raychaudhuri

Poster Session A
Sunday, November 12th
9:00AM-11:00AM

Abstract #0503

https://acrabstracts.org/abstract/spinal-inflammation-a-dominant-pathology-in-psoriatic-arthritis-characterization-and-quantification-by-in-vivo-18f-fdg-total-body-pet-ct-imaging/

This study aimed to identify and characterize the spectrum of spinal inflammation in patients with PsA using PET/CT.

Twenty-five patients with PsA were prospectively recruited (19 male; mean age 51.4±16.4 years; 8 had inflammatory back pain). A total body (TB) ^{18}F-FDG PET/CT was performed at a single-time point.

PET abnormalities were found in 21 (84%) of the participants. Most changes were observed in atlantoaxial, apophyseal, costovertebral/costotransverse, and sacroiliac joints (Figs. 1,2).

Increased ^{18}F-FDG suggesting spinal enthesitis was the most common finding (20/25 patients), observed in cervical, thoracic, and lumbar spine in 14, 15, and 17 patients respectively. Total spine inflammatory load by patient was on average 7.3 ±3.1 rSUVmax.

WHY IMPORTANT?

This study shows that spinal enthesitis is frequent in PsA even in the absence of symptoms. There might be a potential role of PET/CT in diagnosis and quantification of spinal disease.

POLLING QUESTION

How would asymptomatic spinal enthesitis progress and what is its clinical significance?

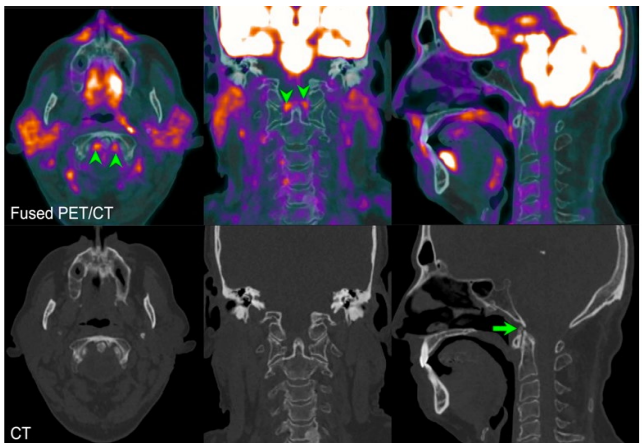


Figure 1. Fused 18F-FDG PET/CT sections (top row) and their corresponding low-dose CT (bottom row) extracted from TB-PET/CT for a 62-year-old man with PsA in axial (left), coronal (middle) and sagittal (right) views. Images demonstrate intense FDG uptake with rSUVmax 1.7 at the alar ligaments (arrowheads)

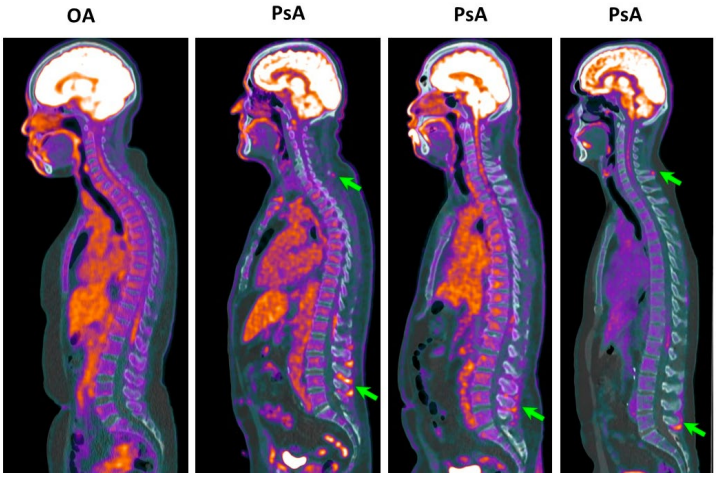


Figure 2. Enthesitis at multiple levels in the spine (green arrows) with or without sacroiliiitis is an interesting finding in the psoriatic arthritis (PsA) patients by total body the PET-CT imaging. Whereas in osteoarthritis (OA) spinal inflammation could not be detected. Involvement of the inter-/supra-spinous ligament are marked by the green arrows.

The Association Between Sonographic Imaging Phenotype and Response to Treatment in Patients with Psoriatic Arthritis

Jessica Gutierrez Manjarrez

Abstract Session
Sunday, November 12th
2:00PM-3:30PM

Abstract #0746

https://acrabstracts.org/abstract/the-association-between-sonographic-imaging-phenotype-and-response-to-treatment-in-patients-with-psoriatic-arthritis/

This study investigated correlations between ultrasound (US) phenotypes in PsA and clinical features and treatment outcomes.

Patients with active PsA were included before initiating systemic treatment (135 treatment periods; 107 patients). Clinical, laboratory tests, and musculoskeletal US assessments were performed at baseline. Drug persistence and disease activity were assessed at 3-6 months.

High correlations of US synovitis and peritendonitis were observed with swollen joints and physician global assessment (Figure 1). Erosion score was the only US feature associated with drug discontinuation (aHR 1.28, 95%CI 1.03, 1.61).

Higher synovitis, peritendonitis, and entheseal structural scores were associated with significant reductions in Disease Activity in PsA (DAPSA) (Table 1). DAPSA reduction was more pronounced in patients on TNFi.

WHY IMPORTANT?

Sonographic synovitis, peritendonitis, and tenosynovitis correlate with treatment outcomes.

POLLING QUESTION

How often do you find sonographic peritendonitis in patients with PsA?

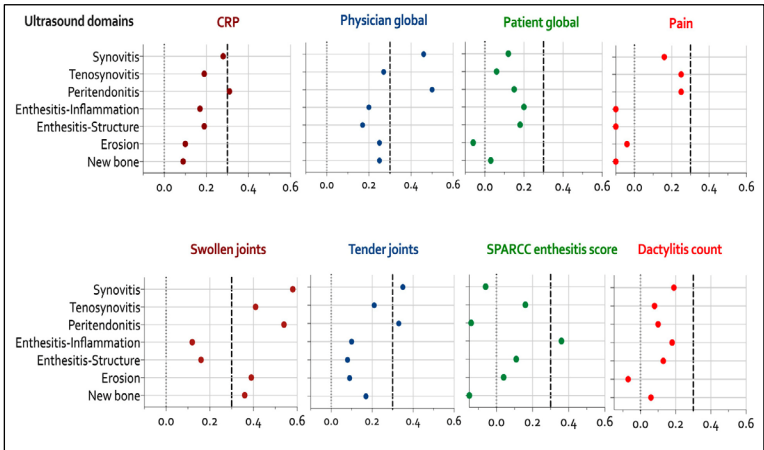


Figure 1 - Pearson correlation coefficients (r) between ultrasound domains and measures of disease activity
CRP-C reactive protein;

Table 1 - The association between baseline ultrasound scores and change in DAPSA score from baseline to follow up visit at 3-6 months - GEE linear regression model

	Multivariate model All patients (N=87)		Multivariate model Patients on TNF inhibitors (N=41)	
	β (95% CI)	P value	β (95% CI)	P value
Total synovitis score	**-3.89 (-7.09, -0.68)**	**0.02**	**-5.26 (-8.84, -1.68)**	**0.004**
Total PTI score	**-3.93 (-7.01, -0.84)**	**0.01**	**-6.11 (-9.85, -2.38)**	**0.001**
Total erosion score	-0.86 (-3.79, 2.07)	0.56	-1.68 (-3.56, 0.20)	0.08
Total NBF score	1.20 (-2.83, 5.22)	0.56	-0.79 (-6.08, 4.51)	0.77
Total tenosynovitis	-4.21 (-8.62, 0.21)	0.06	**-5.18 (-8.73, -1.64)**	**0.004**
Total enthesitis-inflammation	-2.28 (-5.15, 0.57)	0.12	-1.32 (-4.68, 2.04)	0.44
Total enthesitis-structure	**-2.91 (-5.75, -0.06)**	**0.045**	**-3.21 (-6.37, -0.07)**	**0.045**

**Models are adjusted for medication class (targeted DMARD vs. conventional DMARD) and prior exposure to tDMARDs*
CI – confidence intervals; NBF- new bone formation; PTI- peritenon inflammation
Ultrasound scores are standardized.

The Window of Opportunity in Psoriatic Arthritis: Similar to Rheumatoid Arthritis?

Selinde Snoeck Henkemans

Abstract Session
Monday, November 13th
2:00PM-3:30PM

Abstract # 1641

https://acrabstracts.org/abstract/the-window-of-opportunity-in-psoriatic-arthritis-similar-to-rheumatoid-arthritis/

This study investigated if early initiation of DMARDs in patients with PsA is associated with better outcomes.

All DMARD-naïve patients from the DEPAR cohort with a new diagnosis of PsA were included (n=855). Patients were categorized into three groups according to treatment delay from symptoms onset: <12 weeks, 12-52 weeks, and < 52 weeks delay.

The > 52 weeks delay group was significantly less likely to achieve MDA and DAPSA remission over three years of follow-up than the other two groups (Figure 1). This group also scored significantly worse on HAQ-DI than those with <12 weeks delay. Radiographic progression did not differ between the different groups.

WHY IMPORTANT?

Patients with less treatment delay were more likely to achieve better clinical outcomes. This highlights the importance of early referral of these patients.

POLLING QUESTION

What factors do you think are associated with late treatment initiation in PsA?

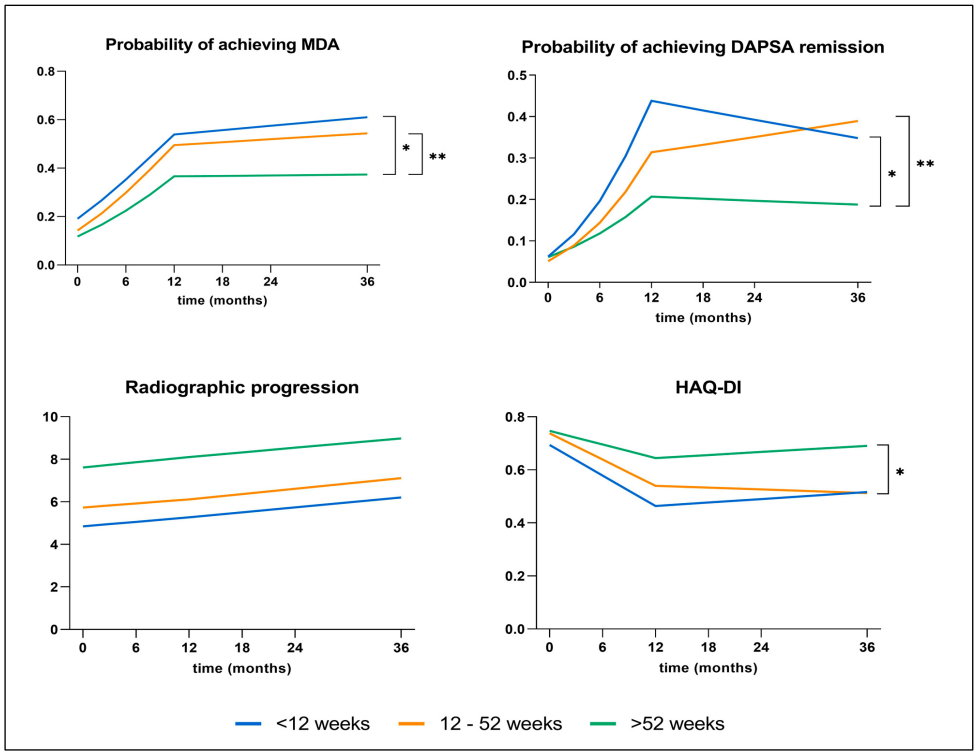


Figure 1. Probability of achieving MDA and DAPSA remission, and radiographic progression and functional ability over 3 years. *Indicates a significant difference between the >52 weeks delay and early diagnosis group, ** indicates a significant difference between the >52 weeks delay and late diagnosis group.

CLINICAL

- Sam Groothuizen, MD
- PhD Candidate at Amsterdam UMC
- Young GRAPPA Member
- Research focus: clinical trials, development of PsA, biomarkers

LinkedIn: Sam Groothuizen - PhD Candidate - Amsterdam UMC | LinkedIn

What Are the Characteristics of a Cost-Effective Psoriatic Arthritis Biomarker Test? An Early Health Technology Assessment

Nick Bansback

Poster Session A
Sunday, November 12th
9:00AM-11:00AM

Abstract #0168

https://acrabstracts.org/abstract/what-are-the-characteristics-of-a-cost-effective-psoriatic-arthritis-biomarker-test-an-early-health-technology-assessment

The aim of this study was to identify the performance metrics needed for a cost-effective diagnostic PsA biomarker. A Markov model was used following a cohort of patients with moderate psoriasis in which PsA was prevalent but unrecognized. Candidate biomarker tests were used at baseline, and when positive patients received conventional DMARDs and biologic treatment. Linear changes in HAQ and PASI scores would parallel disease progression.

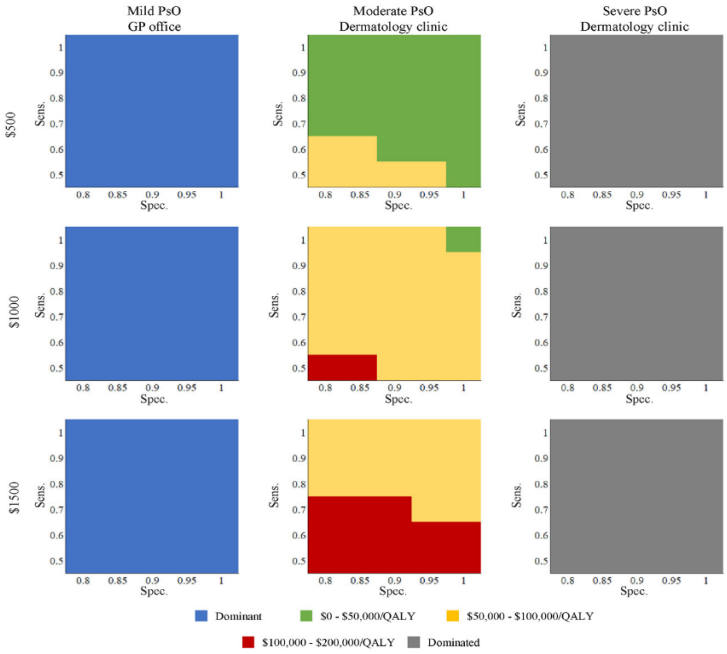
A 500$ biomarker test with 70% sensitivity and 80% specificity was associated with an increased cost of 817$ and 0.02 QALY (quality-adjusted life year) per patient compared to no screening. Sensitivity could be as low as 60% if specificity was at least 88% to be cost-effective. A 1000$ test would not be considered cost-effective unless it is “near-perfect”.

WHY IMPORTANT?

With many biomarkers being studied, it is important to also consider the cost-effectiveness before they can be used in routine clinical practice.

POLLING QUESTION

Do you think the cost-effectiveness needs to be investigated before more research is conducted into new biomarkers?



Characteristics of Difficult-To-Treat Psoriatic Arthritis: A Comparative Analysis

Cecile Philippoteaux

Abstract Session
Sunday, November 12th
2:00PM-3:30PM

Abstract #0777

https://acrabstracts.org/abstract/characteristics-of-difficult-to-treat-psoriatic-arthritis-a-comparative-analysis/

This retrospective study aimed to characterise difficult to treat (D2T) PsA using the EULAR definition and to study a sub-group of patients with more stringent predefined criteria.

If patients fail ≥2 b/tsDMARDs with different mechanisms of action, they are considered D2T. If they fail ≥2 b/tsDMARDs in less than 2 years follow-up, then they are considered very D2T. Characteristics between both groups and non-D2T patients were compared.

150 PsA patients were included, with 49 D2T and 101 non-D2T.

At baseline, a significant difference was seen in axial involvement (43.8% in D2T and 26.0% in non-D2T) and structural damage (76.2% in D2T and 51.0% in non-D2T). Furthermore, in multivariate analysis, D2T patients had more bDMARD discontinuation due to poor cutaneous disease control (OR 2.75, 95%CI 1.23-6.14).

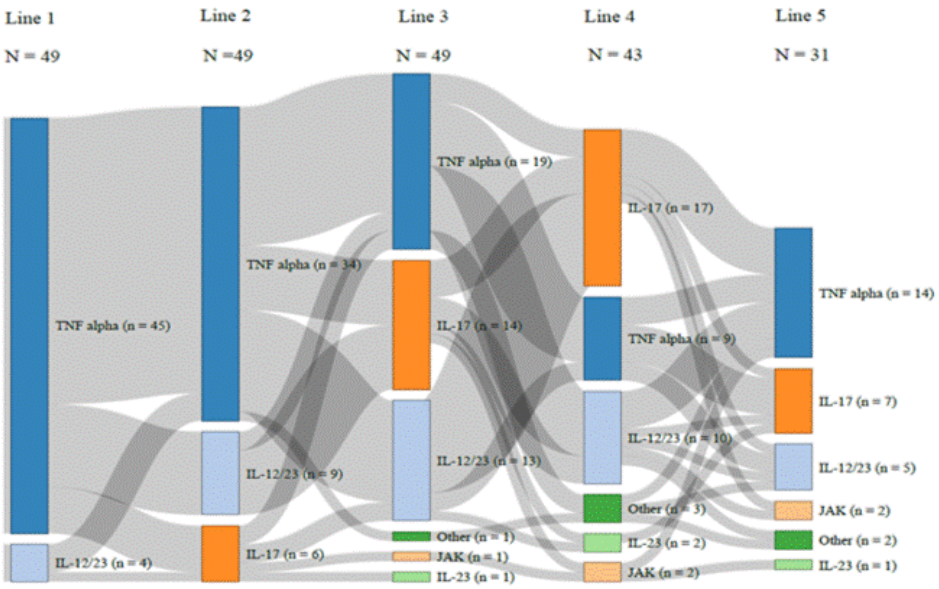
Very D2T PsA represented only a small proportion of patients (17 in total), in which obesity and axial involvement were more prevalent.

WHY IMPORTANT?

A clear definition of D2T PsA is lacking. Defining D2T PsA is important so this sub-set of patients can be included in future clinical trials and epidemiologic studies.

POLLING QUESTION

What is your experience with D2T PsA in clinical practice? Is a specific type of patient more prone to therapy failure?



Abbreviations: JAK: JAK inhibitors (tofacitinib, upadacitinib); IL 12/23: IL 12/23 inhibitors (ustekinumab, guselkumab); IL 17: IL 17 inhibitors (secukinumab, ixekinumab) Other: abatacept, rituximab. TNF alpha: TNF alpha inhibitors (infliximab, certolizumab, golimumab, adalimumab, etanercept).

Identifying Distinct Phenotypes in Psoriatic Arthritis: A Study from the Psoriatic Arthritis Research Consortium (PARC) Cohort

Paras Karmacharya

Abstract Session
Monday, November 13th
2:00PM-3:30PM

Abstract #1642

https://acrabstracts.org/abstract/identifying-distinct-phenotypes-in-psoriatic-arthritis-a-study-from-the-psoriatic-arthritis-research-consortium-parc-cohort/

This study aimed to identify distinct PsA phenotypes using baseline disease characteristics in the PsA Research Consortium (PARC) Cohort.

After imputation of missing values and dimensionality and collinearity reduction, similar patient phenotypes were grouped by hierarchical clustering. The optimal number of clusters was determined by the tree method. After analysing 21 clinical variables of 529 patients, five distinct phenotypic clusters were identified:

- Cluster 1: low disease activity, joint counts and PROs (50.09%)
- Cluster 2: moderate disease activity, higher BMI and joint counts compared to 1 (36.86%)
- Cluster 3: severe psoriasis, higher guttate, palmoplantar, inverse, genital, nail psoriasis and highest mean BMI (5.10%)
- Cluster 4: dactylitis, relatively low joint counts, worse PROs (0.37%)
- Cluster 5: very high disease activity, highest joint counts, body surface area involved with psoriasis and PROs (7.56%)

WHY IMPORTANT?

To better target different treatments to specific patients, it is important to distinguish distinct disease phenotypes.

POLLING QUESTION

Do you think it is necessary to identify distinct phenotypes in the treatment of PsA? And can this help to achieve higher treatment response?

Baseline characteristics	Overall (N=529)	Cluster 1 (N=265)	Cluster 2 (N=195)	Cluster 3 (N=27)	Cluster 4 (N=2)	Cluster 5 (N=40)	†p-value
Age	50.17 (13.69)	50.19 (14.49)	51.10 (12.73)	45.55 (14.24)	47.50 (9.19)	48.63 (12.38)	0.327
Female	282 (56.29%)	120 (47.81%)	128 (68.45%)	10 (41.67%)	2 (100.00%)	22 (59.46%)	<0.0001
Race							0.011
White	444 (92.12%)	226 (91.87%)	171 (95.00%)	22 (95.65%)	2 (100.00%)	23 (74.19%)	
Other	38 (7.88%)	20 (8.13%)	9 (5.00%)	1 (4.35%)	0 (0.00%)	8 (25.81%)	
Ethnicity							0.019
Not Hispanic/Latino	404 (76.37%)	208 (78.49%)	152 (77.95%)	21 (77.78%)	1 (50.00%)	22 (55.00%)	
Hispanic/Latino	28 (5.29%)	8 (3.02%)	14 (7.18%)	0 (0.00%)	0 (0.00%)	6 (15.00%)	
Other	12 (2.27%)	6 (2.26%)	5 (2.56%)	1 (3.70%)	0 (0.00%)	0 (0.00%)	
Clustering variables							
BMI	30.3 (7.3)	28.58 (6.19)	32.42 (7.77)	32.44 (9.64)	28.60 (8.26)	29.36 (6.61)	<0.0001
TJC	5.7 (8.3)	2.05 (3.10)	6.38 (6.90)	8.70 (10.21)	1.50 (2.12)	24.25 (10.90)	<0.0001
SJC	3.3 (5.5)	1.10 (2.21)	3.30 (3.74)	4.15 (4.22)	1.50 (0.71)	16.88 (8.58)	<0.0001
BSA	2.5 (6.8)	1.20 (3.17)	1.99 (4.03)	4.70 (7.02)	2.50 (3.54)	12.52 (18.24)	<0.0001
Enthesitis count	0.7 (1.2)	0.30 (0.70)	0.97 (1.31)	0.93 (1.30)	1.00 (1.41)	1.82 (1.82)	<0.0001
Dactylitis count	0.3 (1.3)	0.13 (0.48)	0.29 (0.93)	0.26 (0.59)	6.50 (9.19)	1.62 (3.49)	<0.0001
Pt pain	4.4 (2.9)	2.30 (1.77)	6.33 (2.03)	4.59 (2.44)	7.00 (4.24)	8.06 (2.29)	<0.0001
Pt global	3.9 (2.8)	1.89 (1.58)	5.80 (1.94)	4.07 (2.64)	6.75 (3.18)	7.29 (2.19)	<0.0001
Pt fatigue*	5.2 (2.7)	3.49 (2.25)	7.06 (1.87)	5.56 (2.26)	6.50 (2.12)	7.47 (2.15)	<0.0001
Axial disease	122 (23.1%)	62 (23.40%)	37 (18.97%)	7 (25.93%)	1 (50.00%)	15 (37.50%)	0.0857
Plaque PsO	225 (42.5%)	104 (39.25%)	76 (38.97%)	17 (62.96%)	1 (50.00%)	27 (67.50%)	0.0011
Inverse PsO	18 (3.4%)	0 (0.00%)	0 (0.00%)	16 (59.26%)	0 (0.00%)	2 (5.00%)	<0.0001
Guttate PsO	8 (1.5%)	1 (0.38%)	0 (0.00%)	7 (25.93%)	0 (0.00%)	0 (0.00%)	<0.0001
Palmoplantar PsO	19 (3.6%)	8 (3.02%)	8 (4.10%)	2 (7.41%)	0 (0.00%)	1 (2.50%)	0.5741
Genital PsO	7 (1.3%)	0 (0.00%)	0 (0.00%)	7 (25.93%)	0 (0.00%)	0 (0.00%)	<0.0001
Pustular PsO	2 (0.4%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (100.00%)	0 (0.00%)	<0.0001
Nail PsO	147 (27.8%)	60 (22.64%)	44 (22.56%)	16 (59.26%)	0 (0.00%)	27 (67.50%)	<0.0001
Uveitis	30 (5.7%)	19 (7.17%)	6 (3.08%)	0 (0.00%)	0 (0.00%)	5 (12.50%)	0.0614
IBD	8 (1.5%)	3 (1.13%)	0 (0.00%)	3 (11.11%)	1 (50.00%)	1 (2.50%)	0.0001
Prior biologic use	206 (38.9%)	86 (32.45%)	82 (42.05%)	11 (40.74%)	1 (50.00%)	26 (65.00%)	0.0011
Elevated CRP	144 (27.2%)	38 (14.34%)	75 (38.46%)	7 (25.93%)	1 (50.00%)	23 (57.50%)	<0.0001

Sex Differences in Perceptions of Psoriatic Arthritis Disease Impact, Management, and Physician Interactions: Results from a Global Patient Survey

Lihi Eder

Poster Session B
Monday, November 13th
9:00AM-11:00AM

Abstract #1217

https://acrabstracts.org/abstract/sex-differences-in-perceptions-of-psoriatic-arthritis-disease-impact-management-and-physician-interactions-results-from-a-global-patient-survey/

This post hoc analysis of an online survey study assessed sex differences in perceptions of disease impact and patient-physician interactions. 1286 PsA patients (52% female) were included, and results were stratified post hoc by sex.

More females had anxiety, osteoarthritis, tried steroids and were taking any DMARD. More females reported negative impact on physical activity and emotional well-being. Furthermore, more females reported emotional distress, stopped social activities and went on permanent work disability. More males reported lower work productivity.

Males switched treatment more often due to potential serious side effect concerns and symptoms being under control, while females reported more switching due to joint symptoms and side effects.

More women were very satisfied with communication and discussed treatment goals with their rheumatologists.

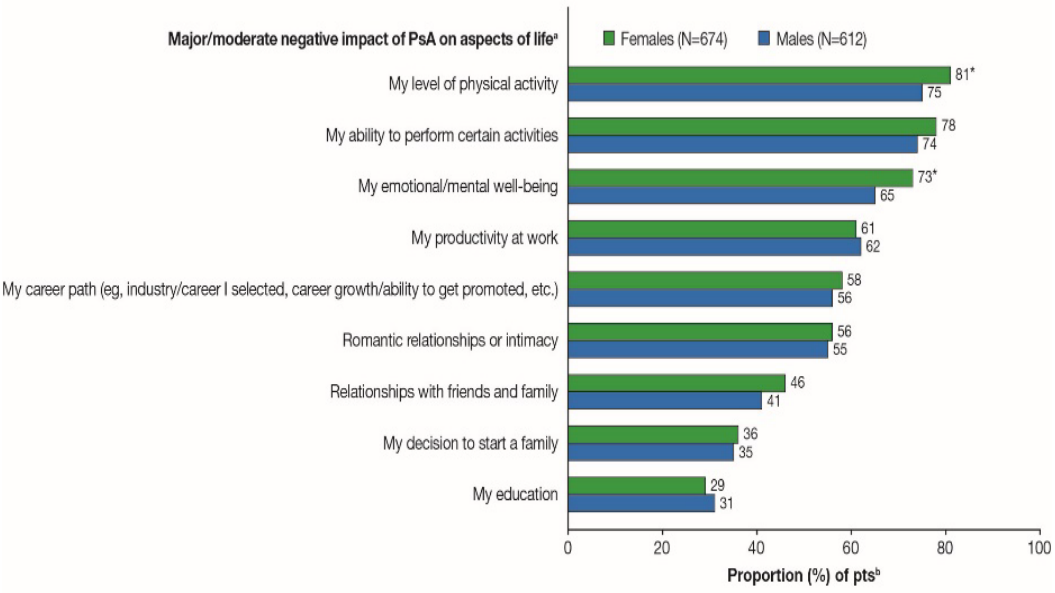
WHY IMPORTANT?

Women with PsA have more severe disease activity and lower health-related qualify of life than men. It is important to consider the impact of sex on patient's disease experience.

POLLING QUESTION

Do you consider the impact of sex in a patient's experience when you discuss their symptoms in your clinic?

Fig. Major/moderate negative impacts of PsA for female vs male pts



*p < 0.05 for females vs males
[a]How much of a negative impact, if any, has PsA had on each of the following aspects of your life?
[b]% based on weighted n (adjusted for size of each country's adult population)
N, number of pts that answered question; pts, patients

TREATMENT

- Zheni Stavre, MD
- Assistant Professor, Rheumatology, UMass Chan Medical School
- Y-GRAPPIAN member
- Early PsA pathogenesis

Twitter: @ZheniGSta
LinkedIn: https://www.linkedin.com/in/zheni-stavre/

Sex of the Patient Affects Response to Advanced Therapies in Psoriatic Arthritis: Meta-analysis of Data from Randomized Controlled Trials

Lihi Eder

Abstract Session
Monday, November 13th
4:00PM-4:10PM
Ballroom 20A

Abstract # 1687

https://acrabstracts.org/abstract/sex-of-the-patient-affects-response-to-advanced-therapies-in-psoriatic-arthritis-meta-analysis-of-data-from-randomized-controlled-trials/

A systematic literature review and meta-analysis was conducted to compare male and female participants in randomized controlled trials (RCTs) for PsA.

Out of 52 trials with 21,769 participants, the average distribution of male and female participants was roughly equal. However, limited RCTs provided sex-disaggregated data for baseline characteristics (17.3%), efficacy endpoints (30.7%), and safety endpoints (3.8%). Female patients had more severe baseline PsA symptoms, while male patients had higher psoriasis area and CRP levels. Male patients exhibited a significantly higher probability of achieving minimal disease activity (MDA) with certain advanced therapies, including IL-17 inhibitors, IL-23 inhibitors, TNF inhibitors, and JAK inhibitors. Variability was observed in achieving ACR response criteria, with male patients generally having higher ACR20 and ACR50 response probabilities across different therapy classes.

In conclusion, female patients in RCTs were less likely to attain efficacy endpoints in various advanced therapy classes, emphasizing the need for future studies to provide sex-disaggregated data for both baseline and endpoint data.

WHY IMPORTANT?

Future PsA clinical trials need to report sex-specific data for more comprehensive understanding and improved treatment strategies.

POLLING QUESTION

Will your next PsA randomized clinical trial be ready to analyse data based on sex?

16-Week Results from FOREMOST, a Placebo-Controlled Study Involving Oligoarticular Psoriatic Arthritis Treated with Apremilast

Philip J. Mease

Abstract Session
Monday, November 13th
4:00PM - 5:30PM

Abstract # 1691

https://acrabstracts.org/abstract/16-week-results-from-foremost-a-placebo-controlled-study-involving-oligoarticular-psoriatic-arthritis-treated-with-apremilast/

The FOREMOST study focused on oligoarticular PsA which can significantly impact the quality of life despite limited joint involvement. This phase 4 trial assessed the efficacy of apremilast (APR) in patients with limited joint involvement, defined as 2-4 swollen and 2-4 tender joints. The study included patients with early PsA (disease duration ≤5 years) and randomized them to receiving APR or a placebo for 24 weeks, with an early escape option at Week 16. The primary endpoint was to achieve minimal disease activity in joints (MDA-Joints) at Week 16, with secondary endpoints assessing disease activity, pain, and patient assessment.

APR was more effective in achieving MDA-Joints compared to placebo, and more patients met the secondary endpoints with APR. Furthermore, patients with 2-4 sentinel joints also showed similar MDA-Joints response rates with APR. A higher percentage of pts with base line joint count ≤4 shifted to a joint count of >4 with placebo vs APR.

Overall, the study demonstrated that APR provides better disease control for early oligoarticular PsA compared to placebo.

WHY IMPORTANT?

Apremilast is effective in establishing disease control in patients with early (disease duration ≤5yrs) oligoarticular PsA.

POLLING QUESTION

Would you consider apremilast as a first-line treatment in patients with oligoarticular PsA?

Table 1. Clinical and Quality-of-Life Outcomes at Week 16

	Sentinel[a] Joints			All Joints (Exploratory Analysis)		
	PBO n=105	APR n=203	Difference (95% CI)	PBO n=105	APR n=203	Difference (95% CI)
Primary endpoint						
MDA-Joints[b], n (%)	16.8 (16.0)	68.8 (33.9)	18.5% (8.9, 28.1) *P*=0.0008	8.3 (7.9)	43.2 (21.3)	13.6% (5.9, 21.4) *P*=0.0028[d]
Secondary endpoints						
cDAPSA REM/LDA[c], n (%)	54.4 (51.8)	142.6 (70.2)	18.6% (7.0, 30.2) *P*=0.0017	40.0 (38.0)	122.5 (60.3)	22.5% (10.7, 34.3) *P*=0.0004[d]
PASDAS Good/ Moderate Response, n (%)	43.9 (41.8)	123.8 (61.0)	19.7% (7.7, 31.8) *P*=0.0016[b]	42.8 (40.8)	120.3 (59.3)	19.0% (7.0, 31.1) *P*=0.0023[d]
PsAID-12, LS mean (SE) change from baseline				-0.4 (0.2)	-1.5 (0.2)	-1.0 (-1.5, -0.6) *P*<0.0001[d]
PtGA ≤20, n (%)				20.1 (19.1)	61.7 (30.4)	11.8% (1.7, 22.0) *P*=0.0286[d]

Percentages are based on the number of patients in the Full Analysis Set.
[a]Sentinel joints defined as joints affected at baseline. [b]MDA-Joints is a composite of TJC ≤1 and SJC ≤1 plus achieving 3 of the following: psoriasis BSA ≤3%, patient assessment of pain VAS (0–100-mm) ≤15, PtGA (0–100-mm) ≤20, HAQ-DI ≤0.5, and LEI ≤1. [c]REM: ≤4, LDA: >4 but ≤13.
[d]Nominal *P*-value.
APR, apremilast; BSA, body surface area; cDAPSA, clinical disease activity index for psoriatic arthritis; CI, confidence interval; HAQ-DI, health assessment questionnaire disability index; LDA, low disease activity; LEI, Leeds enthesitis index; MDA, Minimal Disease Activity; PASDAS (0–10), PsA Disease Activity Score; PBO, placebo; PsAID-12 (0–10), PsA Impact of Disease; PtGA, Pt Global Assessment of Disease activity (0–100 mm VAS); REM, remission; SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale.

Neutrophil Levels Associate with Early Improvement in Spinal Pain and Week 24 Multi-Domain Disease Control During Guselkumab Treatment in Active Psoriatic Arthritis: Post Hoc Pooled Analyses of Two Phase 3 Randomized Controlled Trials

Thomas Macleod

Poster Session C
Tuesday, November 14th
9:00am – 11:00AM

Abstract # 2233

https://acrabstracts.org/abstract/neutrophil-levels-associate-with-early-improvement-in-spinal-pain-and-week-24-multi-domain-disease-control-during-guselkumab-treatment-in-active-psoriatic-arthritis-post-hoc-pooled-analyses-of-two-ph/

This post-hoc analysis of the DISCOVER-1&2 clinical trials aimed to explore the relationship between blood neutrophil levels (peripheral blood absolute counts and neutrophil to lymphocyte ratio-NLR) and clinical outcomes in patients with PsA treated with the IL-23p19-subunit inhibitor guselkumab (GUS).

GUS significantly reduced neutrophil levels as early as week 4, and these reductions were associated with a higher likelihood of achieving important measures of disease control in PsA, such as ACR50, PASDAS low/very low disease activity (LDA/VLDA), and resolution of dactylitis, but not enthesitis at week 24. However, no associations were observed between baseline neutrophil levels and early improvements in various peripheral PsA domains.

Interestingly, lower baseline neutrophil levels were associated with greater improvement in spinal pain in patients with axial involvement, suggesting a potential role of neutrophils in mediating axial over peripheral symptoms. Further research is needed to explore these relationships more comprehensively.

WHY IMPORTANT?

IL-23 inhibition leads to quick reductions in neutrophil levels, correlating with improvement in axial over peripheral symptoms in PsA.

POLLING QUESTION

Do you think there is a differential role for neutrophils in axial vs peripheral PsA?

Table. Association of W4 Changes in Neutrophil Levels with Achievement of Clinical Outcomes at W24 in GUS-Treated Pts

Achievement at W24	$\Delta_{BL \rightarrow W4}$Neutrophil Count OR† (95% CI)	$\Delta_{BL \rightarrow W4}$NLR OR† (95% CI)
BASDAI20 (in 194 pts with axPsA)	1.15 (0.93, 1.41)	1.34 (1.03, 1.73)**
ACR50	1.11 (1.00, 1.24)**	1.14 (1.02, 1.28)**
PASDAS LDA/VLDA (in 740 pts with BL PASDAS>3.2)	1.12 (1.00, 1.25)*	1.07 (0.95, 1.21)
Dactylitis resolution (in 319 pts with BL dactylitis)	1.22 (1.02, 1.46)**	1.18 (0.98, 1.43)*
Enthesitis resolution (in 473 pts with BL enthesitis)	1.08 (0.95, 1.23)	0.97 (0.85, 1.10)

†ORs>1 indicate an association between greater reductions in neutrophil levels and higher likelihood of achieving clinical outcomes at W24. Adjusted for BL levels, GUS regimen, prior TNFi use, and BL use of conventional synthetic DMARDs.
*p<0.1, **p<0.05.

Bimekizumab Impact on Core Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Domains for Patients with Psoriatic Arthritis: 52-Week Results from Four Phase 3 Studies

Joseph Merola

Poster Session B
Monday, November 13th
9:00AM-11:00AM

Abstract # 1433

https://acrabstracts.org/abstract/bimekizumab-impact-on-core-group-for-research-and-assessment-of-psoriasis-and-psoriatic-arthritis-grappa-domains-for-patients-with-psoriatic-arthritis-52-week-results-from-four-phase-3-studies/

Bimekizumab (BKZ), an antibody that targets IL-17F and IL-17A, demonstrated significant clinical efficacy in patients with PsA and psoriasis. This study aimed to assess BKZ's effectiveness across the key domains outlined by the Group for Research and Assessment of Psoriasis and PsA (GRAPPA), including peripheral arthritis, axial disease, enthesitis, dactylitis, skin psoriasis, nail psoriasis, and PsA-related conditions like uveitis and inflammatory bowel disease (IBD). The analysis included two phase 3 trials in PsA and two in axial spondyloarthritis (axSpA).

Patients were either given subcutaneous BKZ or placebo every four weeks. By week 52, most patients had completed the study, and improvements were observed in all GRAPPA domains for BKZ-treated patients. These improvements were consistent between patients who were biologic DMARD-naïve and TNFi-inadequate responders. The study suggested that BKZ is effective in treating axial disease in PsA, and there were low rates of IBD and no cases of uveitis observed.

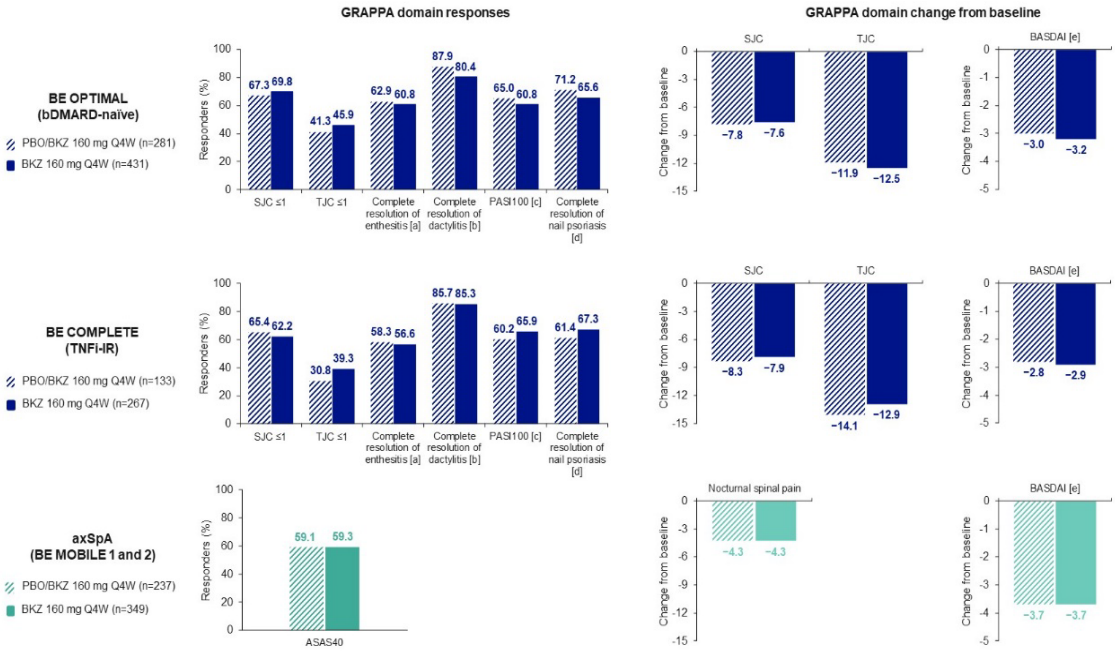
In summary, BKZ treatment led to sustained improvements in multiple domains in patients with PsA, with potential efficacy in the axial domain, and had a favourable safety profile.

WHY IMPORTANT?

Bimekizumab shows sustained improvement through week 52 in multiple PsA domains, including axial disease in both bDMARD-naïve and TNFi-IR patients.

POLLING QUESTION

Would Bimekizumab offer an added benefit compared to IL-17Ai in the treatment of PsA?



Randomized set from BE OPTIMAL, BE COMPLETE (including data from BE VITAL), BE MOBILE 1, and BE MOBILE 2. ASAS40 data are pooled from BE MOBILE 1 and 2. [a] In patients with enthesitis at baseline (LEI >0); [b] In patients with dactylitis at baseline (LDI >0); [c] In patients with ≥3% body surface area affected by psoriasis at baseline; [d] In patients with nail psoriasis at baseline (mNAPSI >0); [e] In patients with BASDAI ≥4 at baseline. ASAS40: Assessment in Spondyloarthritis international Society 40% improvement; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; GRAPPA: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MI: multiple imputation; nr-axSpA: non-radiographic axSpA; NRI: non-responder imputation; PASI100: 100% improvement in Psoriasis Area and Severity Index; PBO: placebo; Q4W: every four weeks; r-axSpA: radiographic axSpA; SJC: swollen joint count; TJC: tender joint count; TNFi-IR: TNF-α inhibitor-inadequate responders.

TREATMENT

- Andre Ribeiro, MD
- Rheumatologist at Women's College Hospital, University of Toronto, Canada
- Education subcommittee
- Research focus: musculoskeletal ultrasound and enthesitis

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Effectiveness of Dose Reduction and Withdrawal Strategies of TNF Inhibitors in Psoriatic Arthritis and Axial Spondyloarthritis: Long Term Extension of the DRESS-PS Study

Amy Peeters

Abstract Session
Sunday, November 12th
2:00PM-3:30PM

Abstract #0775

https://acrabstracts.org/abstract/effectiveness-of-dose-reduction-and-withdrawal-strategies-of-tnf-inhibitors-in-psoriatic-arthritis-and-axial-spondyloarthritis-long-term-extension-of-the-dress-ps-study/

TNFis are effective for PsA and axSpA but come with the risk of infections and high costs. The DRESS-PS study showed that a Treat-To-Target (T2T) tapering strategy in PsA and axial SpA patients was as effective as T2T without tapering in achieving Low Disease Activity (LDA) at 12 months, but with reduced TNFi use. This study extended the DRESS-PS study by 12 months of observation, and all patients could undergo tapering. The primary outcomes were disease activity and TNFi use, with secondary outcomes focused on functional status and quality of life.

Out of 122 patients, 114 participated in the extension. The LDA rate at 24 months was 67% for the intervention group and 72% for the control group. Most patients (89%) tried tapering during follow-up. TNFi use at 24 months was 66% for the intervention group and 77% for the control group. Functional status and quality of life were similar for both groups.

Comparing protocolized tapering to the routine care tapering in the original control arm showed no difference in LDA after tapering (70% vs. 72%), but there was a significant difference in TNFi use (52% vs 77%).

In conclusion, T2T tapering of TNFi is effective for up to two years, but TNFi use was higher at 24 months than at 12 months. Tapering seems less frequent in routine care of this patient group when compared to RA.

WHY IMPORTANT?

T2T tapering of TNFi in PsA and axial SpA can be an effective and safe approach for up to 2 years, decreasing costs and risks associated with full dosage.

POLLING QUESTION

Based on the findings from the DRESS-PS study extension, would you consider implementing T2T tapering of TNFi in your clinical practice for patients with PsA and axial SpA?

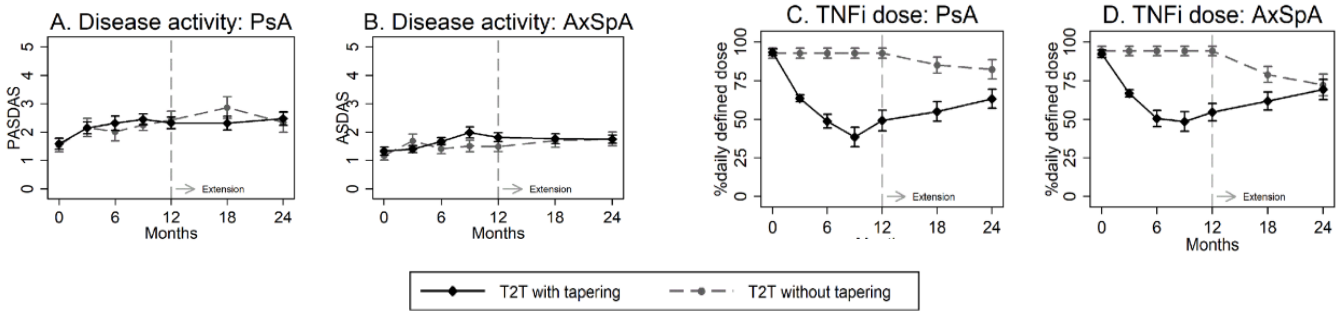

Figure 1: Mean disease activity presented as PASDAS in patients with PsA (A) and ASDAS in patients with AxSpA (B) and mean TNFi dose presented as percentage of daily defined dose in patients with PsA (C) and patients with AxSpA (D), between T2T with tapering and T2T without tapering.

Removal of Methotrexate in Patients with Active Psoriatic Arthritis with Newly Induced Ustekinumab Treatment Leads to a Delayed Response in DAPSA and DAS28 Within the First 16 Weeks

Michaela Koehm

Poster Session B
Monday, November 13th
9:00AM-11:00AM

Abstract #1440

https://acrabstracts.org/abstract/removal-of-methotrexate-in-patients-with-active-psoriatic-arthritis-with-newly-induced-ustekinumab-treatment-leads-to-a-delayed-response-in-dapsa-and-das28-within-the-first-16-weeks/

Methotrexate (MTX) is commonly used to treat active PsA. The study aimed to determine the effects of combining MTX with ustekinumab (UST) versus UST alone, focusing on early treatment response within the first 16 weeks.

173 patients with active PsA (defined as TJC≥4, SJC≥4 [68/66 joint count], and DAS28≥3.2) were randomized to either UST+MTX or UST+Placebo. The main outcomes analyzed were disease activity measures and early response rates at weeks 4, 16, and 24.

Patients who discontinued MTX at the start of the study had slightly less low disease activity (LDA) and remission rates in DAS28-CRP compared to those who continued MTX (DAS28-CRP 21.62% vs. 25.59%, respectively). This difference was more evident at week 4 (10.81% vs. 25.59%), but by weeks 16 and 24, the response rates were similar between the groups.

Combining MTX with UST is as effective as UST alone for treating active PsA in the long-term. However, continuing MTX treatment in the early phase of UST therapy (first 12-16 weeks) can enhance early response rates.

WHY IMPORTANT?

For patients with PsA starting UST, continuing MTX for the initial 12-16 weeks can provide a better early response, but by 24 weeks, the efficacy of UST is evident regardless of MTX usage.

POLLING QUESTION

Do you usually continue or stop MTX right after starting Ustekinumab? Will this study change your current protocol?

Figure 1: LDA and Remission rates for DAS28-CRP and DAPSA response at weeks 4, 16, and 24 in the cohort of PsA patients with MTX pretreatment and either discontinuation at the start of UST treatment or continuation of both MTX and UST

Izokibep Demonstrates Major Disease Control on ACR70, PASI100 and Enthesitis Resolution in Patients with Active Psoriatic Arthritis Treated Through 46 Weeks

Philip J. Mease

Abstract Session
Monday, November 13th
4:00PM-5:30PM

Abstract #1688

https://acrabstracts.org/abstract/izokibep-demonstrates-major-disease-control-on-acr70-pasi100-and-enthesitis-resolution-in-patients-with-active-psoriatic-arthritis-treated-through-46-weeks/

IL-17 inhibition has proven effective in various domains of PsA. Izokibep is an IL-17A inhibitor with high IL-17A binding affinity, a small molecular size and an albumin attachment site. This phase 2 trial reports on baseline to 46-week efficacy and safety outcomes.

Patients were given Izokibep at doses of either 80 mg or 40 mg every two weeks (Q2W) up to 46 weeks or until the study terminated. Post 16 weeks, the placebo group switched to 80 mg Q2W.

Of the 135 patients randomized, the majority in the 80 mg group and those who switched from placebo achieved DAPSA low disease activity/remission and minimal disease activity (MDA) by week 46 (65% and 71%, respectively).

Izokibep 80 mg resulted in significant disease control, with 52% achieving ACR70, 71% reaching PASI 100, and 89% having complete enthesitis resolution by LEI.

The drug was well-tolerated with a safety profile in line with other approved IL-17A inhibitors.

WHY IMPORTANT?

This study shows Izokibep's efficacy and safety over a 46-week period with a high enthesitis resolution rate.

POLLING QUESTION

Would you consider favouring Izokibep over other medications in a patient with severe enthesitis?

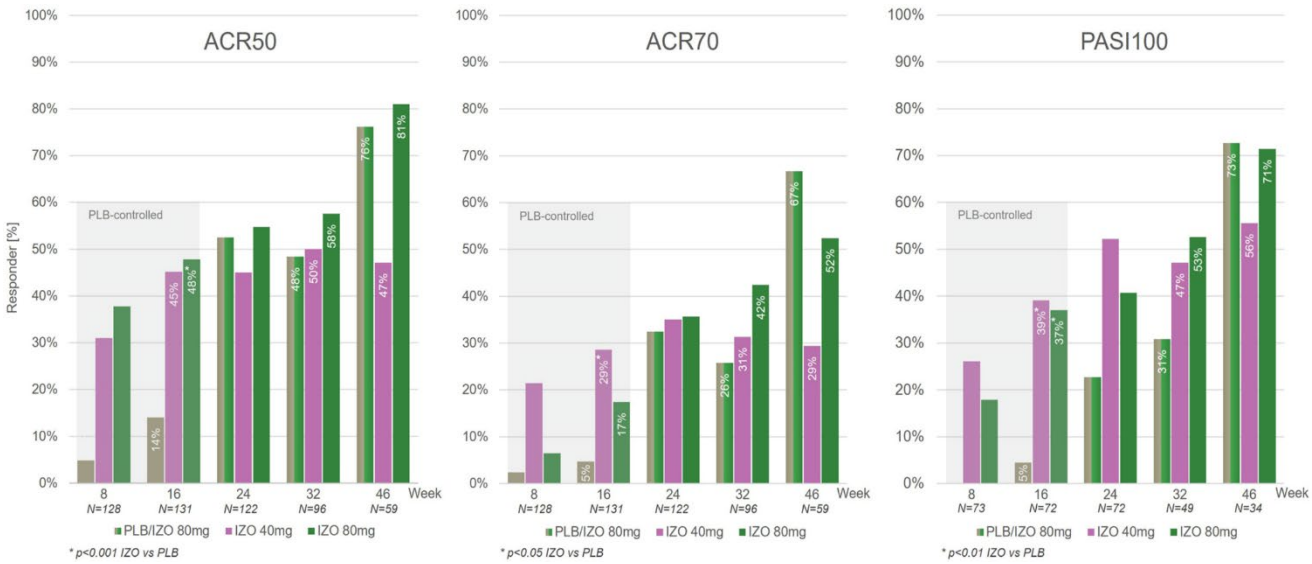

Figure 1. High Levels of ACR50, ACR70, and PASI100 Scores Obtained at Week 46

Efficacy and Safety of Intravenous Secukinumab for the Treatment of Active Psoriatic Arthritis: 16- and 52-Week Results from a Randomized, Double-Blind, Phase 3 Study

Alan Kivitz

Abstract Session
Sunday, November 12th
2:00PM-3:30PM

Abstract #0776

https://acrabstracts.org/abstract/efficacy-and-safety-of-intravenous-secukinumab-for-the-treatment-of-active-psoriatic-arthritis-16-and-52-week-results-from-a-randomized-double-blind-phase-3-study/

This randomized, double-blind, placebo-controlled phase 3 study, INVIGORATE-2, aimed to examine the long-term effects, safety, and tolerability of intravenous (IV) secukinumab (SEC) in patients with active PsA over a 52-week period.

Participants were randomized to receive either IV SEC or placebo. At Week 16, those on placebo switched to IV SEC and treatment continued until Week 52. A higher proportion of patients receiving IV SEC than placebo achieved ACR50 at Week 16 (31.4% vs 6.3%). By Week 52, both groups exhibited similar ACR50 response rates (58% and 64%).

IV SEC demonstrated greater efficacy in secondary outcomes compared to placebo at Week 16: 22.5% vs. 5.3% for MDA, 48% vs. 6.4% for PASI90, 59.3% vs. 32.4% for dactylitis resolutions, and 55.6% vs. 39.1% for enthesitis resolution. By Week 52, both groups had comparable outcomes.

The incidence of adverse events was similar for both groups. For the entire study period on IV SEC, 63.4% reported any adverse event, 5.9% a serious adverse event, and 1.9% discontinued treatment due to adverse events.

In conclusion, IV SEC has been shown to be a safe and effective long-term treatment for active PsA, with a profile consistent with subcutaneous SEC.

WHY IMPORTANT?

IV secukinumab offers a promising long-term treatment option for active PsA, with maintained efficacy up to 52 weeks and a safety profile consistent with SC administration.

POLLING QUESTION

How likely are you to consider IV SEC instead of SC SEC for patients with active PsA?

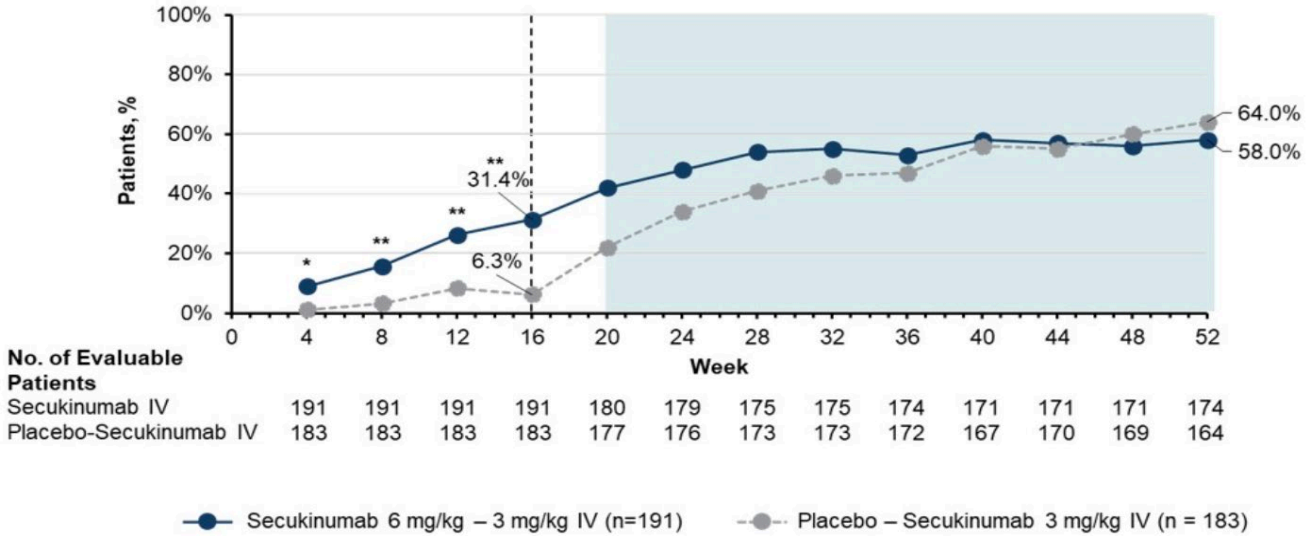

Figure 1. Proportion of patients with PsA who achieved ACR50 through Week 16 (nonresponder imputation) and through Week 52 (observed data)

YOU ARE INVITED!

Join us for the next in our series of GRAPPA Virtual Congress Highlights on November 27th where we will be highlighting the hottest topics from the ACR 2023 Congress in San Diego. This event is open to all so tell your colleagues and help spread the word.

Registration is available here.