EULAR 2023

DO NOT MISS HIGHLIGHTS IN PSORIATIC DISEASE

JUNE 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 EULAR congress in Milan.

Roxana Coras

Sam Groothuizen

Zheni Stavre

NEWSLETTER

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Y-GRAPPiAns

Young Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

TRANSLATIONAL SCIENCE

- Roxana Coras, YGRAPPA member
- Rheumatology Trainee, Cedars Sinai Medical Center, Los Angeles, California
- Leader of the Y-GRAPPA Website Group
- Biomarkers of disease activity in Psoriasis and Psoriatic Arthritis

Linkedin: Roxana Coras
Twitter: @roxana_coras

Exploring levels of protein biomarkers in response to treatment for psoriasis and psoriatic arthritis

D. D. Gladman

E-poster

Abstract # AB1110

http://scientific.sparx-ip.net/archiveeular/?searchfor=Exploring%20levels%20of%20protein%20biomarkers%20in%20response%20to%20treatment%20for%20psoriasis%20and%20psoriatic%20arthritis&c=a&view=1&item=2023AB1110

The objective of this study was to evaluate the levels of CXCL10, MMP3, S100A8, CCL2, and ACP5 in serum of psoriasis (PsO) and PsA patients before and after treatment with biologic agents (TNFi and IL-17i).

CXCL10, MMP3 3, S100A8, ACP5, and CCL2 significantly decreased after TNFi treatment in PsA patients. CXCL10 and ACP5 significantly increased after IL-17i treatment in PsA patients. There were no significant differences between treated and untreated PsO patients.

WHY IMPORTANT?

Identifying biomarkers of response to different treatments can help us choose personalized treatments for our patients, since not all patients respond to the same therapies.

POLLING QUESTION

Do you think we will be able to practice personalized medicine in the future?

Single cell RNA-seq dissection of the synovial fluid in psoriatic arthritis patients identifies myeloid subsets related to treatment response with bDMARDS

R. Tzemach

06/01/2023 11:35-11:45
Room Amber 3+4

Abstract# OP0110

http://scientific.sparx-ip.net/archiveeular/?c=s&view=1&searchfor=OP0110

Psoriatic arthritis (PsA) is a complex chronic inflammatory disease involving aberrant activation of the innate and the adaptive immune systems. A comprehensive map of the myeloid compartment of the synovial fluid is lacking. The inflammatory pathways leading to anti TNF or other bDMARDs resistance are unknown and biomarkers to predict treatment response are scarce.

A total of 91,837 cells from 33 PsA Patients (11 naive, 22 under cDMARDs and bDMARDs: 9 anti-TNF and other 9 bDMARDs) and 7 controls (OA) were analyzed.

The synovial fluid myeloid compartment of PsA patients was composed of intermediate monocytes (CD14+ CD16+); TREM2 macrophages; conventional dendritic cells: cDC1 (XCR1, CLEC9A), cDC2 (CD1c, CLEC10A) and migratory DCs (mDC: CCR7, LAMP3, IDO1).

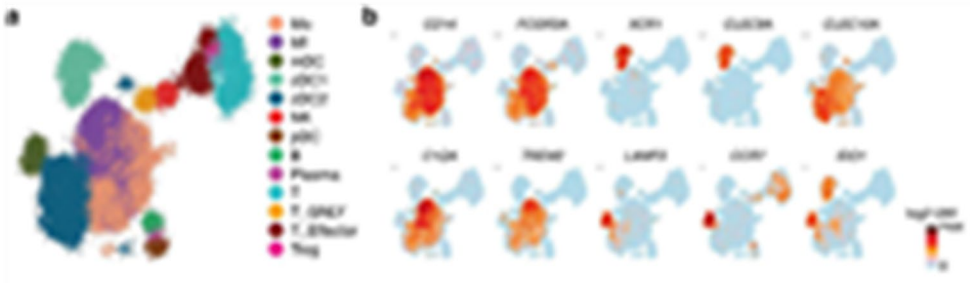
The study identified a unique cluster of cDC2 and monocytes with shared molecular signature, characteristic of anti TNF or other bDMARDs non-responders. These clusters demonstrated a high expression of interferon signature genes (ISG15, ISG20, IFI27, IFI6, IFIT3, STAT1) and genes related to the immunoproteasome (PSMB9, PSMB8, PSME2, PSME1, POMP).

WHY IMPORTANT?

This study identified clinically significant cell-subsets within the cDC2 and monocytes populations associated with anti -TNF or other bDMARDs non-response, revealing potential biomarkers and future therapeutic targets.

POLLING QUESTION

Do you think studying the cells in the synovial fluid is relevant? Or would you prefer the synovial tissue?



DNA methylation patterns in CD4+ T cells discern skin psoriasis from psoriatic arthritis

V. Natoli

06/02/2023 11:15-11:25
Room Amber 1+2

Abstract # OP0100

http://scientific.sparx-ip.net/archiveeular/?searchfor=DNA%20methylation%20patterns%20in%20CD4+%20T%20cells%20discern%20skin%20psoriasis%20from%20psoriatic%20arthritis&view=1&c=a&item=2023OP0100

Effector T-cells have been showed to play a key role in the pathogenesis of psoriasis and psoriatic arthritis. Recent studies linked altered DNA methylation with T-cell dysregulation and phenotypical variation between patients.

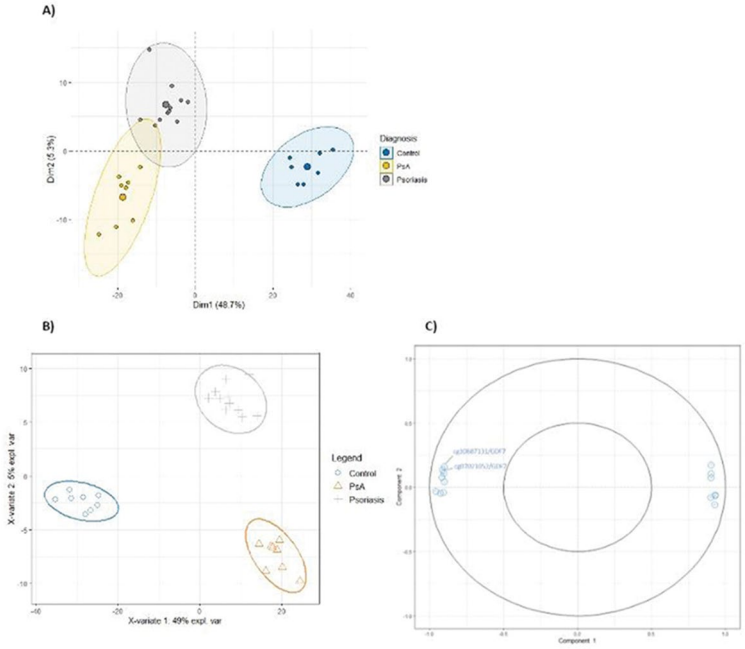
This study aimed to identify disease-associated DNA methylation signatures in CD4+ T-cells from psoriasis and PsA patients as compared to healthy controls. These could then be used as diagnostic and/or prognostic biomarkers and inform future treatment. 820 differentially methylated positions (DMPs) affecting 433 genes in CD4+ T-cells were detected when healthy controls were compared to psoriasis and PsA patients. Based on DMP analyses, groups segregated in principal component (PCA) or partial least-squares discriminant analyses (PLS-DA) (Figure 1). Separation in PLS-DA was centrally influenced by two CGs (cg07021052, cg10687131) localized in GDF7 (Growth and Differentiation factor 7), which affects T-cell regulatory factors FOXP3 and CTLA4. DNA methylation profiles in CD4+ T-cells discriminate between controls, skin psoriasis and PsA.

WHY IMPORTANT?

As DNA methylation signatures may predict disease progression from psoriasis to PsA, they may be applied for molecular patient stratification towards future individualized treatment and care.

POLLING QUESTION

Do you think this method will make it to clinical practice?



CLINICAL

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

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

The impact of 6-month delay in diagnosis on clinical and functional status in the PsA patients under bDMARD treatment: results from Treasure database

G. Ayan

06/01/2023 at 14:45 – 15:45 in Posters Hall B-11

Abstract # POS0879

https://scientific.sparx-ip.net/archiveeular/index.cfm?searchfor=psoriatic arthritis&view=3&c=a&item=2023POS0879

It has previously been shown that a diagnostic delay is associated with worse prognosis in PsA. This study aimed to evaluate the impact of a 6-month diagnostic delay in PsA patients undergoing bDMARD therapy.

Data from the Treasure database were used. The time between symptom to diagnosis was known in 865 patients, with a diagnostic delay of over 6 months being observed in 72.4% of cases. This group also had a longer time to the initiation of bDMARD therapy, a higher prevalence of sacroiliitis, and a higher ASDAS-CRP and VAS-Physician Global scores. Interestingly, dactylitis was more common in patients with less than 6 months of delay in diagnosis.

WHY IMPORTANT?

Nearly 75% of PsA patients using bDMARDs experienced a diagnostic delay exceeding 6 months, significantly prolonging the time until treatment initiation. This delay underscores the importance of improving early PsA detection.

POLLING QUESTION

What do you think could be changed in our current clinical practice to expedite PsA diagnosis?

Table 1. Demographic and Clinical Characteristics of Patients with/without diagnostic delay

	Patients with diagnostic delay< 6 monthsn=238	Patients with diagnostic delay> 6 monthsN=627	P
Current Age (y)	45 (38-57)	47 (40-57)	0.09
Gender (male) n, (%)	89 (37.4)	200 (31.9)	0.13
Delay in diagnosis, month	3.0 1.0-4.9)	24.0 (11.9-61.0)	**<0.001**
Disease duration (symptom-bDMARD initiation)	2.4 (0.8-7.1)	6.1 (3.3-6.1)	**<0.001**
Disease duration (diagnosis-bDMARD initiation)	2.3 (0.6-7.1)	2.5 (0.7-6.2)	0.61
BMI	28.1 (24.6-32.0)	28.0 (24.9-31.9)	0.62
Smoking (ever)	119 (50.6)	289 (47.2)	0.37
CCI (≥1), n (%)	47 (19.7)	127 (20.3)	0.62
ASDAS-CRP	3.45 (2.77-4.08)	3.62 (3.14-4.25)	**0.011**
BASFI Score (0-10)	4.6 (2.2-6.2)	4.7 (3.4-5.9)	0.52
BASFI category > 4	92 (61.7)	307 (71.4)	**0.028**
EQ5D score	11 (9-11)	11 (10-12)	**0.026**
HAQ-DI score	0.64 (0.40-1.0)	0.63 (0.50-0.80)	0.76
HAQ-DI category<0.50.5-1.0> 1.0	37 (28.0)58 (43.9)37 (28.0)	68 (17.6)241 (62.4)77 (19.9)	**0.002**
VAS-Physician global	70 (50-80)	70 (60-80)	**0.003**
Sacroliitis according to mnY, n (%)	80 (46.2)	238 (57.3)	**0.014**
Dactylitis, n (%)	64 (31.2)	105 (19.1)	**<0.001**

Specific AI-generated pattern of tender joints and tenderness at enthesial sites are predictive for objective detection of musculoskeletal inflammation in psoriasis patients

M. Köhm

06/01/2023 at 14:45 – 15:45 in Posters Hall B-13

Abstract # - POS0881

https://scientific.sparx-ip.net/archiveeular/index.cfm?searchfor=psoriatic arthritis&view=3&c=a&item=2023POS0881

Up to 30% of patients with psoriasis (PsO) develop PsA. As defined approaches for early PsA detection are still lacking, this study aimed to perform an AI-based cluster analysis in a cohort of at-risk PsO patients to identify clinical markers for early PsA diagnosis. Clinical data sets from the XCITING study were used. The AI-based analysis used the attributes joint and entheses tenderness to detect clinical profiles for early detection of inflammatory musculoskeletal disease. The analysis identified seven different cluster types that were tested for their significance to predict the presence or absence of MSK inflammation. Three clusters showed a significant correlation: cluster 2 (no major findings) was associated with no inflammation, whereas cluster 4 ('feet-type') and 6 (predominance at PIP and DIP joints) were associated with MSK inflammation at the hands.

WHY IMPORTANT?

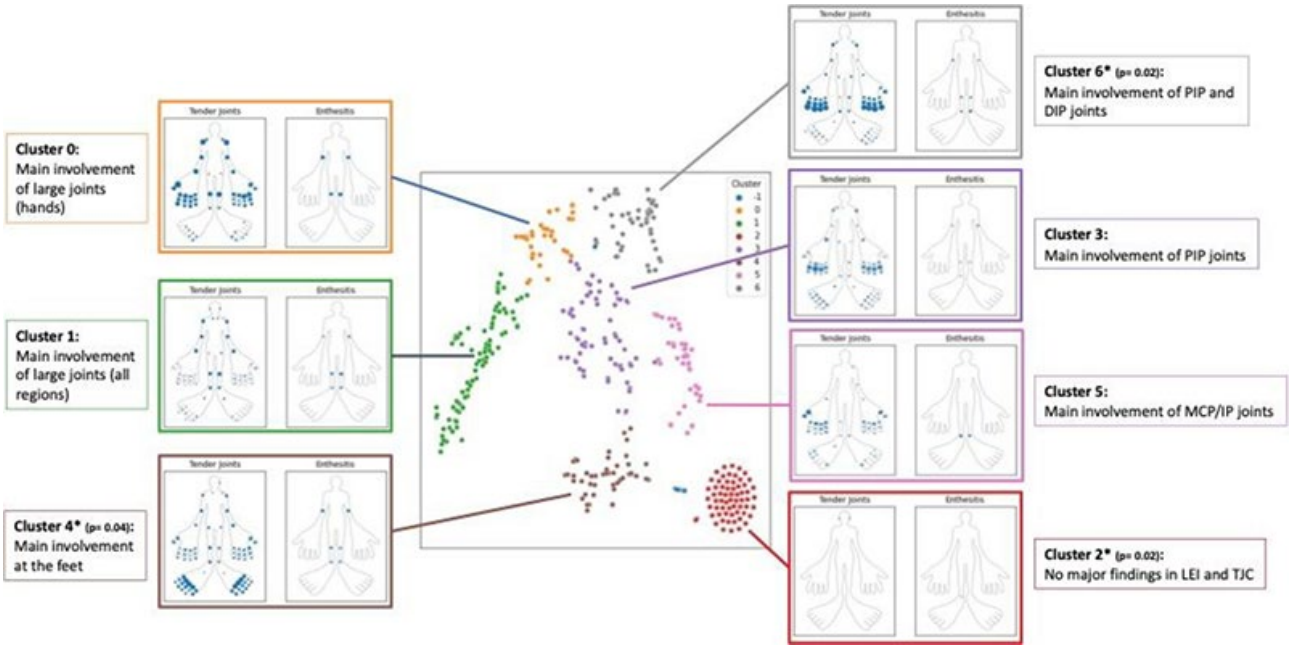
AI can help to recognize clusters of clinical signs associated with specific disease profiles, which may lead to new insights into disease classification and into mechanisms driving pathogenesis.

POLLING QUESTION

How do you think AI could contribute to clinical decision-making in the near future?

Table 1. Results of the cluster analysis

Cohort	Cluster	P-Value	Odds Ratio	CI	n=402
No major findings in LEI and TJC	Cluster 2	**0.02**	0.53	[0.31, 0.91]	64
Main involvement at the feet	Cluster 4	**0.04**	2.0	[1.03, 4.06]	48
Main involvement of PIP and DIP joints	Cluster 6	**0.02**	2.2	[1.10, 4.31]	50
Combination of other clusters	0 + 1+3 + 5	0.53	0.87	[0.58, 1.31]	240



Biologic therapies for psoriasis and psoriasis arthritis affect on future risk for developing major adverse cardiovascular events

A.Dotan

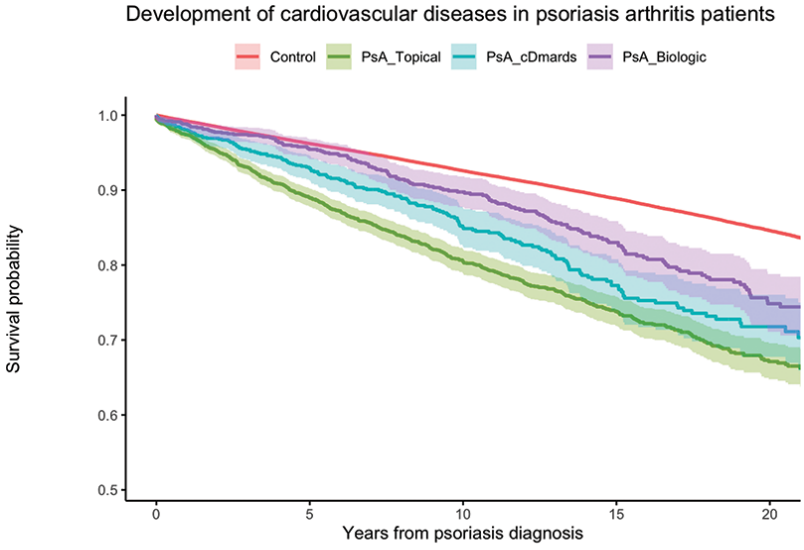
06/03/2023 at 10:30 – 11:30 in Posters Hall G-20

Abstract # - POS1525

https://scientific.sparx-ip.net/archiveeular/?c=a&searchfor=psoriasis&view=2&item=2023POS1525

Psoriasis (PsO) and PsA are strongly associated with cardiometabolic syndrome and its consequences. This study assessed the risk of developing major adverse cardiovascular events (MACE) in patients with pre-existing PsO and PsA under various treatment regimes.

This retrospective study used Israeli health maintenance databases. Patients were categorized according to diagnosis (control, PsO, or PsA) and treatment type (topical, cDMARDs, or bDMARDs). The study, which included 287,392 patients, used adjusted Cox proportional hazards regression analyses to assess the risk of MACE. A higher MACE risk was seen in PsO patients treated with topical therapies and cDMARDs (topical HR 1.1, CI 1.02-1.1, p-value <0.001, cDMARDs HR 1.2, CI 1.0-1.5, p-value 0.05), while bDMARD-treated PsO patients exhibited no significant MACE risk difference compared to controls. Conversely, the MACE risk was increased in all PsA treatment groups.



Number at risk

Control	230293	172470	112925	62795	20560
PsA_Topical	2704	2088	1463	906	388
PsA_cDmards	976	757	476	277	125
PsA_Biologic	1020	826	602	381	188

Cumulative number of events

Control	6	7980	13396	16946	18955
PsA_Topical	16	284	461	563	626
PsA_cDmards	1	65	118	152	168
PsA_Biologic	3	44	88	126	155

WHY IMPORTANT?

It is crucial to investigate which therapies can lower the presence of cardiometabolic comorbidities associated with PsO and PsA. This study's findings suggests that treatment choices may have a significant impact on patients' cardiovascular health.

POLLING QUESTION

Do you think studies examining the impact of different therapies on associated comorbidities should be considered when selecting a specific therapy for your patient?

Biologic therapies for psoriasis decrease future risk for developing psoriatic arthritis

A. Watad

06/02/2023 at 09:30 – 10:30 in Posters Hall G-6

Abstract # - POS1607

https://scientific.sparx-ip.net/archiveeular/index.cfm?searchfor=psoriatic%20arthritis&view=3&c=a&item=2023POS1607

Psoriasis (PsO) is an inflammatory skin disorder affecting 2-4% of the global population. PsO is often followed by the development of PsA, which can severely impact the quality of life. This retrospective study investigated the impact of different biological therapies for PsO in relationship to the prevention of PsA.

Real-world data from the 'Meuhedet' Israeli health organization, which included 58,671 PsO patients, were used. Patients were grouped according to their treatment regimens: topical therapy, csDMARDs and bDMARDs. Time-dependent Cox proportional hazard models were employed to calculate the risk of developing PsA. The risk of developing PsA in PsO patients treated with csDMARDs was significantly higher compared to those using topical therapy (HR 2.76, CI 2.19-3.48, p-value <0.001). On the contrary, the risk was decreased in patients treated with bDMARDs compared to topical therapy (HR 0.62, CI 0.42-0.90, p-value <0.014).

WHY IMPORTANT?

Given that up to 30% of PsO patients develop PsA, understanding the impact of different PsO treatments on preventing PsA is crucial.

POLLING QUESTION

Do you believe certain treatments can prevent the progression from PsO to PsA?

Prediction of psoriatic arthritis tool (PRESTO): development and performance of a new scoring system for psoriatic arthritis risk

L. Eder

06/01/2023 at 12:00 – 12:05 in Poster Tour Room 3

Abstract # - POS0019

https://scientific.sparx-ip.net/archiveeular/index.cfm?searchfor=psoriatic arthritis&view=3&c=a&item=2023POS0019

Early diagnosis of PsA is paramount for an ideal therapeutic response. Employing tools for the identification of psoriasis (PsO) patients at high-risk for developing PsA could improve early detection and thus improve patient care. This study aimed to develop an accurate risk prediction model for the development of PsA among patients with PsO.

Data from PsO patients from the longitudinal IPART cohort were analyzed to develop risk prediction models. The analysis included 635 PsO patients, of which 51 and 71 patients developed PsA over 1 and 5 years, respectively. The model showed reasonable accuracy, with a sensitivity and specificity for a 2.5% probability of PsA onset within 1 year of 54.5% and 75%, respectively. The sensitivity and specificity for a 5% probability of PsA onset within 5 years period were 61.1% and 77%, respectively.

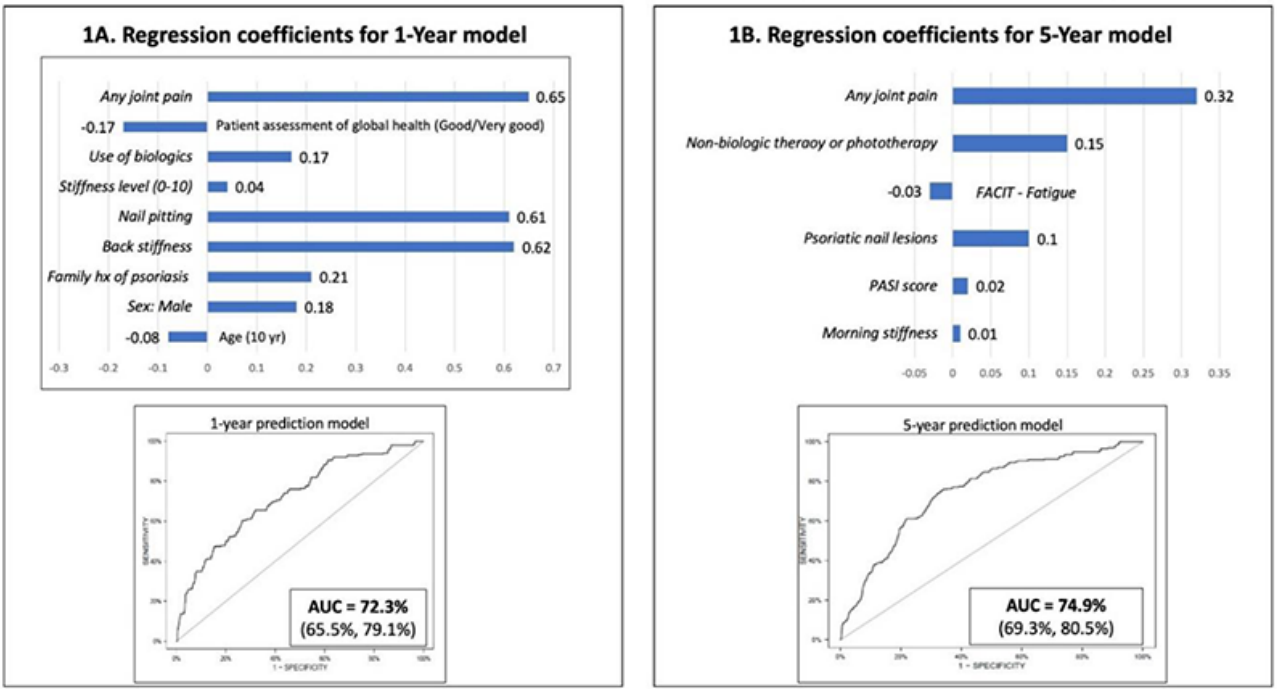
WHY IMPORTANT?

It is important to detect PsA in an early stage to facilitate early intervention. A simple clinical tool to identify at-risk patients would be valuable in clinical practice.

POLLING QUESTION

Do you consider the patient characteristics in PsO patients to estimate whether they have an increased risk of developing PsA?

Figure 1: Prediction Models for the Development of PsA in Psoriasis Within 1-year Period (1A) and Within 5-year Period (1B)



The determinants of radiographic progression in early PsA patients

G.H. Koc

05/31/2023 at 17:05 – 17:15 in South Hall, Session Room 1

Abstract # - OP0065

https://scientific.sparx-ip.net/archiveeular/index.cfm?searchfor=psoriatic arthritis&view=3&c=a&item=2023OP0065

Psoriatic arthritis (PsA) is an inflammatory arthritis often linked with progressive erosive damage and functional impairment. This study aimed to assess baseline clinical parameters as potential determinants for radiographic progression in early PsA patients, with a 2-year follow-up period.

The study analyzed data from the DEPAR study, which included 358 newly diagnosed PsA patients. Overall, 42 patients showed radiographic progression over two years. Baseline clinical determinants associated with radiographic progression were older age, swollen joints, previous erosive damage, a higher joint space narrowing (JSN) score, and a baseline C-reactive protein (CRP) level >1 mg/dl.

WHY IMPORTANT?

Erosive disease is common in PsA and is associated with functional impairment. Therefore, it is important to identify patients at increased risk for further damage.

POLLING QUESTION

Do you think that patients at risk of radiographic progression should be treated more aggressively than others?

Table 1. Baseline clinical parameters for radiographic progression

	Non-progression(n=316)	Progression(n=42)
Age [a]	50 (14)	57 (11)
Gender (Female)(%)	50%	52%
Symptom duration [b]	10 (4-27)	11 (4-35)
Swollen joint count [b]	2 (1-5)	3 (2-5)
Swollen joint count (y/n)(%)	78%	93%
Tender joint count [b]	4 (2-8)	4 (1-8)
Tender joint count (y/n) (%)	89%	83%
CRP [a]	8.50 (13.61)	12.28 (18.4)
CRP* (%)	74%	88%
ESR [b]	10 (5-26)	16 (8-40)
DAPSA [a]	19.3 (10.57)	18.81 (9.55)
Enthesitis (y/n)(%)	44%	50%
ΔmTSS [b]	0 (0-0)	3 (2-5)
mTSS [b]	0 (0-2)	22 (4-48)
JSN [b]	0 (0-1)	13 (1-23)
Erosion score [b]	0 (0-1)	11 (1-21)
Erosive disease (y/n) * (%)	18%	57%

TREATMENT

- Zheni Stavre, MD, Assistant Professor of Medicine/Rheumatology
- UMass Chan Medical SChool
- Y-GRAPPA member
- Neutrophils and PsA

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

Combining MTX Does Not Result in an Additional Efficacy of UST Treatment in Polyarthritic PSA: Subgroup Analysis From a Randomized Placebo-Controlled Investigator Initiated Clinical Trial

M. Köhm

06/02/2023 at 12:25 – 12:30 in Poster Tour Room 10
Abstract #: POS0229

https://scientific.sparx-ip.net/archiveeular/?searchfor=psoriatic%20arthritis&c=a&view=1&item=2023POS0229

In treating PsA, a common practice derived from treatments of rheumatoid arthritis (RA), is the addition of methotrexate (MTX) to biologic therapy.

This investigator-led, randomized, placebo-controlled trial recruited 166 patients with active PsA. They were randomized to either ustekinumab (UST) plus MTX or UST plus placebo. ACR20/50/70 and MDA response rates at week 24 were compared and stratified with respect to the number of affected joints. The main finding was that supplementary MTX had no positive impact on UST efficacy, irrespective of the number of affected joints.

WHY IMPORTANT?

MTX did not enhance the treatment response in patients with PsA treated with UST.

POLLING QUESTION

Would you stop methotrexate upon starting ustekinumab?

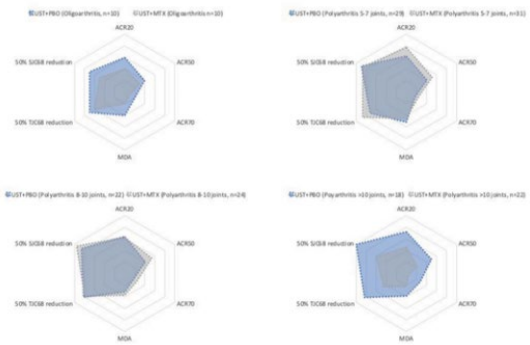


Figure 1. Response to the different treatment regimes, stratified by number of affected joints at Baseline (mITT population)

Treatment Effects of Ixekizumab and Adalimumab at the Individual Digit Level with Nail and Distal Interphalangeal Joint Involvement in Patients with Psoriatic Arthritis

D. Mcgonagle

06/03/2023 at 10:30 – 11:30 in Posters Hall G-21
Abstract #: POS1526

https://scientific.sparx-ip.net/archiveeular/?c=a&searchfor=psoriatic%20arthritis&view=1&item=2023POS1526

Nail disease is present in 41% to 93% of patients with PsA and is strongly linked to adjacent distal interphalangeal joint (DIP) disease. This post-hoc analysis of the SPIRIT-H2H assessed the efficacy of ixekizumab (IXE, N=186) and adalimumab (ADA, N=168) on nail disease.

From the 354 patients included, all had nail involvement and at least one tender or swollen DIP. NAPSI total score >0 and proportions of patients having DIP involvement (tenderness or swelling) were evaluated at baseline and week 24. The IXE treatment group showed a significantly lower prevalence of nail and/or DIP involvement, compared to the ADA group, at week 24.

WHY IMPORTANT?

It is important to study which agents work best to control inflammation in different disease domains to targeted therapy to individual patients.

POLLING QUESTION

Would you consider switch from a TNFi to ixekizumab in patient with PsA with persistent nail and DIP involvement?

Table 1. The proportion (%) of patients with (A) NAPSI >0 and (B) DIP involvement (tenderness or swelling) at Week 24 at the individual digit level among patients treated with either IXE (N=186) or ADA (N=168) who had NAPSI >0 and distal interphalangeal joint involvement at baseline. *p<0.05, †p<0.1, ‡p<0.001 vs ADA, Fisher's Exact test p-value.

	Left Hand				Right Hand					
	Little	Ring	Middle	Fore	Thumb	Thumb	Fore	Middle	Ring	Little
NAPSI >0 (%)Week 24										
IXE Q4WADA Q2W	17.0*27.9	17.6*27.9	14.2†25.5	15.3†27.3	11.4†23.6	15.3†27.3	13.6†25.5	15.3*26.7	15.9†26.7	13.121.2
p-value*	**0.0191**	**0.0276**	**0.0097**	**0.0079**	**0.0039**	**0.0079**	**0.0062**	**0.0113**	**0.0169**	0.0602
Week 52IXE Q4WADA Q2W	10.921.4	10.316.6	10.915.9	10.317.2	9.114.5	12.119.3	9.717.2	10.919.3	7.312.4	10.914.5
p-value*	**0.0128**	0.1304	0.2400	0.0958	0.1547	0.0859	0.0641	0.0538	0.1770	0.3924
DIP involvement (%) Week 24										
IXE Q4W	10.7	11.3	15.8	19.8	17.5	15.8	20.9	21.5	11.9	10.7
ADA Q2W	15.2	20.0	25.5	27.3	24.8	22.4	28.5	30.9	17.0	18.8
p-value*	0.2590	**0.0357**	**0.0319**	0.1249	0.1115	0.1307	0.1312	**0.0495**	0.2168	**0.0459**
Week 52IXE Q4WADA Q2W	1.22.8	2.44.8	7.28.3	5.45.5	1.26.2	1.84.1	4.27.6	4.29.7	4.84.1	1.24.1
p-value*	0.4228	0.3578	0.8322	1.0000	**0.0273**	0.3128	0.2305	0.0703	1.0000	0.1521

Assessment of Pain Outcomes in a Phase 2 Trial of Deucravacitinib in Patients with Active Psoriatic Arthritis

P. J. Mease

06/03/2023 at 10:30 – 11:30 in Posters Hall G-26
Abstract #: POS1536

https://scientific.sparx-ip.net/archiveeular/index.cfm?view=1&c=a&searchfor=deuc&item=2023POS1536

Deucravacitinib (DEUC), is a novel JAK-inhibitor which selectively targets TYK2.

This phase 2 study involved 203 patients with PsA, a condition known to cause pain that impacts patients' daily life and quality of life. Patients were randomized to placebo (PBO), DEUC 6 mg/day, or DEUC 12 mg/day. Three surveys were used to assess pain at baseline and through week 16: Pain VAS, PsAID, and SF-36.

A higher proportion of patients with PsA treated with DEUC reported clinically meaningful improvements in pain when compared with those on PBO.

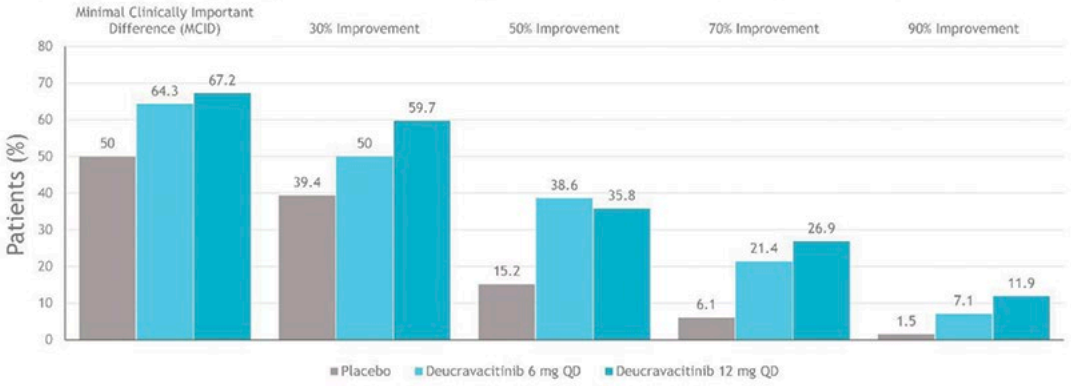
WHY IMPORTANT?

Assessment of pain outcomes is an important indicator of a drug's success in treating PsA, making DEUC a promising treatment option for PsA.

POLLING QUESTION

Are you looking forward to DEUC, a medication targeting a new JAK family member, to treat PsA?

Figure. Percentage of patients reporting improvements in pain (Pain VAS) at week 16



Missing values imputed using nonresponder imputation method. Minimal Clinically Important Difference is defined as ≥10-point reduction in change from baseline, or ≥15% reduction in percent change from baseline on a scale of 0-100.
QD, once daily; VAS, visual analog scale.

DO NOT MISS EULAR 2023 UPDATE IN PSORIATIC DISEASE MANAGEMENT

Recommendation

OPEN ACCESS

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update

2023 UPDATE

Laure Gossec ,[1,2] Xenofon B[illegible]kos,[3] Andreas Kerschbaumer ,[4] Maarten de Wit ,[5] Iain M[illegible],[6] Maxime Dougados,[7] Lotte Primdahl ,[8,9] Dennis G McGonagle,[10,11] D[illegible] Aletaha,[12] Andra Ba[illegible]esc[illegible],[13] Peter V Balint,[14] Heidi Bertheussen,[15] Wolf-Henning Boehncke,[16] [illegible] R [illegible]urmester,[17] Juan D Canete ,[18] Nemanja S Damj[illegible]ov,[illegible] Wenzel Kragstrup,[20,21] Tore K Kvien,[22] Robert B M Land[illegible]ve,[23,24] Rik [illegible]ozef Urbain Lories,[25,26] Helena Marzo-Ortega,[10,11] Den[illegible] P[illegible]dubnyy ,[27,28] Santiago Andres Rodrigues Man[illegible]a ,[29,30] Georg Schett ,[31] Douglas J Veale ,[32] Filip E Van den Bosch,[33] Désirée van der Heijde ,[22,34] Josef S Smolen[35,36]

Presenter: L. Gossec

Time: 03-JUN-2023 @ 12:15

Location: Auditorium