Content #ACR22 DNM Newsletter:

Y-GRAPPiANs

Young Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

This Newsletter was prepared by Y-GRAPPA members.
It highlights some of the very interesting Psoriatic Arthritis abstracts that will be presented in the 2022 ACR meeting in Philadelphia.

Make sure not to miss those

ACR 2022 "DO NOT MISS" HIGHLIGHTS IN PSORIATIC DISEASES

André Ribeiro

Mohamad Bittar

Gizem Ayan

Fabian Proft

COI Disclosures: FP reports research support from Novartis, Eli Lilly and UCB, consultancy fees and speakers bureau from AbbVie, AMGEN, BMS, Celgene, Hexal, Janssen, MSD, Novartis, Pfizer, Roche and UCB. AR reports support for attending meetings and/or traveling from AbbVie. MB, FS, UGG, GA report no potential conflict of interests.

BASIC SCIENCE

*Flavia Sunzini, MD
*Rheumatologist and Clinical Immunologist
*Clinical-Research Fellow and PhD candidate
University of Glasgow, Scotland
*Young GRAPPA member, Newsletter Group
*Research focus: Psoriatic arthritis and Pain

Twitter: @FlaviaSunzini
Linkedin: Flavia Sunzini

IL-23 Induced Growth Differentiation Factor 15 Contributes to Trabecular Bone Loss, but Does Not Affect Skin, Gut or Joint Inflammation in Psoriatic Arthritis

Renée Van der Cruyssen

November 13, 2022,
10:30AM-11:30AM
Oral Number: 1096

https://acrabstracts.org/abstract/il-23-induced-growth-differentiation-factor-15-contributes-to-trabecular-bone-loss-but-does-not-affect-skin-gut-or-joint-inflammation-in-psoriatic-arthritis/

This study demonstrates high levels of Growth Differentiation Factor 15 (GDF15) in patients with SpA. GDF15 levels depend on IL-23 overexpression in mice and humans. The effect of GDF15 is characterised by trabecular bone loss independent from the levels of inflammation.

WHY IMPORTANT?

Remarkable work of weight and bone loss that might explain clinical manifestations independent from the level of inflammation.

POLLING QUESTION

Do you think investigating bone-brain interactions, would be relevant to better understand SpA/PsA pathogenesis?

Figure 1

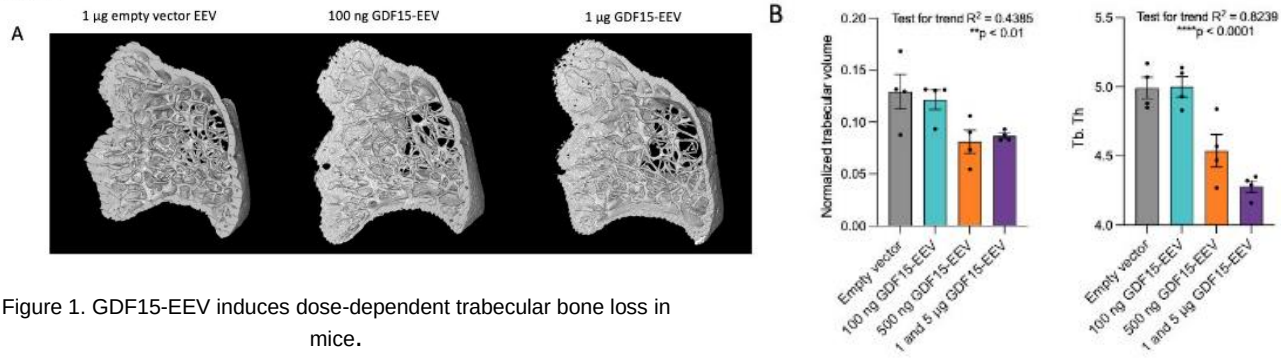


Figure 1. GDF15-EEV induces dose-dependent trabecular bone loss in mice.

Intrinsic STAT1 Deficiency Underlies Proinflammatory Imprint of Naive CD4+ T Cells in SpA

Bilade Cheraqaoui

November 13, 2022,
11:15 AM – 11:25 AM
Oral Abstract
Number: 1097

https://acrabstracts.org/abstract/intrinsic-stat1-deficiency-underlies-proinflammatory-imprint-of-naive-cd4-t-cells-in-spondyloarthritis/

A type 3 immune response characterizes Spondyloarthritis (SpA) onset and pathogenesis. In animal models, the T-cells are more prone to differentiate towards a Th17 phenotype. STAT1/STAT3 unbalance skews cells towards altered differentiation. STAT3 hyperactivity is associated with Th17 expansion in rats and in humans.

WHY IMPORTANT?

This work sheds light on preserved intracellular mechanisms behind pathogenic Th17 cell differentiation.

POLLING QUESTION

Do you think targeting STAT can be a useful therapeutic tool in SpA?

Table 1:

Upstream TF	Premorbid rats		Adult rats	
BRCA1	2,2	-2,2	2,2	-2,2
STAT1	2,0	-1,9	1,6	-0,2
ETS1	1,6	0	1,4	0
STAT3	2,1	1,1	3,7	2,4
	-log(adj p value)	Activation z-score	-log(adj p value)	Activation z-score

RNA-seq performed on mLN naive CD4+ T cells from 3 wk-old B27-rats (n = 7) and controls (n = 5), or 3-mo old B27-rats (n = 7) and controls (n = 7). Upstream transcription factors (TF) predicted to explain differentially enriched genes profile in naive CD4+ T cells from B27-rats, as compared to controls; -log (adj p value) calculated by Fisher's exact test; z-score refers to the activation (red), inhibition (blue) or undefined (white) state of the downstream regulated genes in B27-rats.

Epigenome-Wide Integrative Association Study on Spondyloarthritis and Psoriatic Arthritis

Elena Carnero-Montoro

November 13, 2022,
1:00PM-3:00PM
Poster Number: 1155

https://acrabstracts.org/abstract/epigenome-wide-integrative-association-study-on-spondyloarthritis-and-psoriatic-arthritis/

The authors identified 24 differentially methylated CpG sites (DMS) between SpA and PsA. These sites are not only associated with the pathogenesis, such as HLA-B27 and JAK2-signalling, but also with disease activity and clinical phenotypes. Moreover, DMS were able to distinguish between Axial SpA and PsA, and predict disease activity in SpA.

WHY IMPORTANT?

Stimulating epigenome study on SpA and PsA. Epigenetics has an important regulatory role in the pathogenesis of different diseases. This study fills the gap in the current available literature.

POLLING QUESTION

Do you think an epigenomic signature would be able to better characterize clinical phenotypes and inform clinical decision in the future?

Mechanical Loading-induced BHLHE40 Promotes Inflammatory Arthritis

Dirk Elewaut

November 13, 2022,
10:30AM-11:30AM
Poster Number: 1094

https://acrabstracts.org/abstract/mechanical-loading-induced-bhlhe40-promotes-inflammatory-arthritis/

Mechanical load in synovial fibroblasts induces BHLHE40 gene expression, and the expression of 600 other genes in RA and PsA. BHLHE40 is present in fibroblasts and macrophages promoting joint inflammation, uncoupled with systemic inflammation.

WHY IMPORTANT?

Mechanical load is an essential trigger for PsA, however there is a lack of mechanistic studies. This study describes a new potential regulator of mechanical inflammation.

POLLING QUESTION

Do you think targeting inflammation associated with mechanical stress is an important aspect regarding PsA treatment?

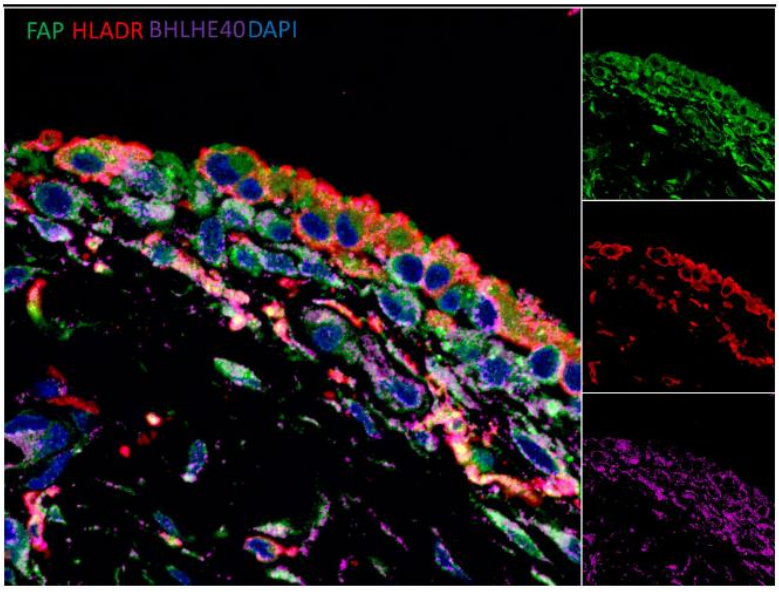


Figure 1: BHLHE40 is widely expressed in human synovium. Synovium obtained from total knee replacement. FFPE samples were stained for synovial macrophages (HLADR+) and fibroblasts (FAP+). Images acquired with the Zeiss LSM 780.

*André Ribeiro, MD
*Rheumatology Fellow at Hospital de Clínicas de Porto Alegre
*Young Grappa member: Participates in the Education Committee, Do Not Miss, ACR Highlights, and Slide Library Projects

https://www.linkedin.com/in/andre-ribeiro-49b093104

Twitter: dr_AndreRibeiro

Toll-like Receptor Ligands Stimulated Monocyte-Derived Langerhans Cell-Like Dendritic Cells Induce Psoriasis-Related Molecules, IL-23 and Delta-Like-4

Rei Takahashi

ABSTRACT NUMBER: 0583
Poster Session B
Sunday, November 13,
9:00 AM - 10:30 AM

https://acrabstracts.org/abstract/toll-like-receptor-ligands-stimulated-monocyte-derived-langerhans-cell-like-dendritic-cells-induce-psoriasis-related-molecules-il-23-and-delta-like-4/

Monocyte-derived Langerhans cell-like dendritic cells (Mo-LCs) are involved in the pathogenesis of psoriasis in murine models. The role of Mo-LCs in the development of psoriasis in humans is still poorly understood due to lack of an optimal method to induce Mo-LCs differentiation. This study found that stimulating CD14+ monocytes with immobilized human notch ligand delta-like (DLL)-1 and DLL-4 induced Mo-LC differentiation. In addition, Mo-LCs produced significant amounts of IL-15 and IL-23, and expressed DLL-4, which are all related to the pathology of psoriasis.

WHY IMPORTANT?

The development of a reproducible method to induce Mo-LCs will allow for better understanding of the role of this cell in the pathology of psoriasis.

POLLING QUESTION

Will Mo-LCs become a future therapeutic target in the management of psoriasis?

Psoriatic Arthritis Disease Subtypes Mediated by CD8 T cells are Phenocopied in a Novel Humanized Murine Model of Psoriasis and Arthritis

Maria de la Luz Garcia-Hernandez

ABSTRACT NUMBER: L04
Late-breaking abstract
Monday, November 14,
9:00 AM - 10:30 AM

https://acrabstracts.org/abstract/psoriatic-arthritis-disease-subtypes-mediated-by-cd8-t-cells-are-phenocopied-in-a-novel-humanized-murine-model-of-psoriasis-and-arthritis/

CD8 T cells have a role in the pathogenesis of PsA, but their roll in driving the disease into different domains is poorly understood. In this research, the authors injected sera and peripheral blood mononuclear cells (PBMCs) from patients with different phenotypes into immunodeficient NSG-SGM3 mice to assess the profile of synovial CD8 T cells. They induced different disease phenotypes, with each phenotype showing a different CD8 T cell profile, indicating that serum factors and CD8 T cells might promote domain specific phenotypes.

WHY IMPORTANT?

A better understanding of the pathogenesis of each PsA domain will allow for the development of more specific therapies.

POLLING QUESTION

Do you believe an individualized treatment approach based on a patient's profile of CD cells, assessed by flow cytometry, will be possible in the near future?

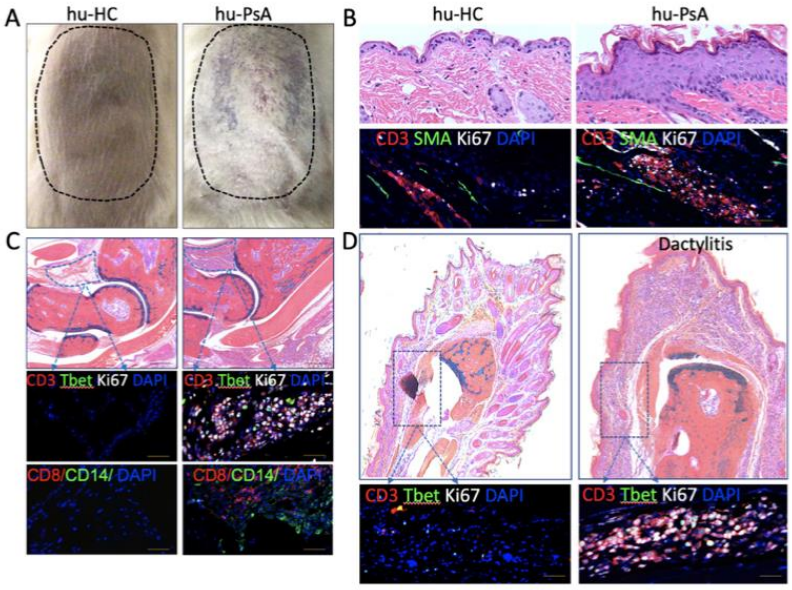


Figure 1. Serum soluble factors and PBMCs are crucial to recapitulate PsA in humanized NSG-SGM3 mice. A) Pictures of skin from hu-PsA mice show psoriasiform lesions in mice injected with serum and PBMCs from PsA patient. B) Histological pictures of hu-PsA mice show increased epidermal thickness and significant accumulation of proliferative $CD3^+$ T cells (CD3: red, Ki67: white, smooth muscle actin (SMA): green), compared to hu-HC. C) Mouse ankles from hu-PsA have considerable synovial inflammation (dotted outline), proliferative type 1 $CD3^+$ T cells and co-localization of CD8 T cell and $CD14^+$ cells. D) hu-PsA developed dactilytis (dotted lines) with proliferative (Ki67-white) type 1 (T-bet-green) $CD3^+$ T cells (CD3-red). 200x magnification pictures were taken with a Zeiss Axioplan microscope and recorded with a Hamamatsu camera. Scale bar = 1000 µm.

CLINICAL

*Ummugulsum Gazel, MD
*Rheumatologist
*Clinical-Research Fellow at University of Ottawa
*Young GRAPPA member
*Participates in GRAPPA MSUS Working Group
and Imaging Library Project

https://www.researchgate.net/profile/Ummugulsum-Gazel

https://www.linkedin.com/in/ummugulsum-gazel/

Diagnostic Delay and Less Intensive Therapy for People with Psoriatic Arthritis Compared with Rheumatoid Arthritis: A Nested Matched Cohort Study from Within the UK National Early Inflammatory Arthritis Audit

William Tillett

ABSTRACT NUMBER: 1613
Oral presentation on
Sunday, November 13,
4:30PM-6:00PM

https://acrabstracts.org/abstract/diagnostic-delay-and-less-intensive-therapy-for-people-with-psoriatic-arthritis-compared-with-rheumatoid-arthritis-a-nested-matched-cohort-study-from-within-the-uk-national-early-inflammatory-arthrit/

This study compared the time elapsed between the onset of symptoms and referral to a rheumatologist between PsA and RA patients, and compared their initial treatments. The authors created a nested matched cohort and patients were included from the National Early Inflammatory Arthritis Audit in England and Wales. Among 2021 PsA patients who were matched to RA patients, 1250 had polyarticular disease. PsA patients had a longer symptom duration before referral and a longer interval between first presentation and getting diagnosed by a Rheumatologist. The diagnostic delay was most evident amongst people with longer symptom duration. Furthermore, a significantly smaller number of PsA patients got DMARDs at baseline than RA patients. During the follow-up, less improvement in disease activity was observed in PsA patients versus RA patients.

WHY IMPORTANT?

As early treatment is highly recommended for a better prognosis in PsA, this study highlights the importance to pay attention to diagnostic delay and to therapy choices in PsA patients.

POLLING QUESTION

In your practice, do you observe a difference between RA and PsA patients regarding the time for diagnosis and treatment intensity?

The Impact of Second-Line Therapeutic on Disease Control After Discontinuation of First Line TNF Inhibitor in Patients with PsA: Analysis from the CorEvitas Psoriatic Arthritis/Spondyloarthritis Registry

Alexis Ogdie

ABSTRACT NUMBER: 1600
Oral presentation on
Sunday, November 13
3:45 PM – 3:55 PM

https://acrabstracts.org/abstract/the-impact-of-second-line-therapeutic-on-disease-control-after-discontinuation-of-first-line-tnf-inhibitor-in-patients-with-psa-analysis-from-the-corevitas-psoriatic-arthritis-spondyloarthritis-regis/

In PsA patients, relative effectiveness of cycling vs switching to a therapy with a different mechanism of action is still unclear. In this longitudinal cohort study, 394 PsA patients who discontinued a 1st line TNFi and started a 2nd line therapy, either another TNFi (cyclers – 52%) or a non-TNFi biologic (switchers – 48%), were included. Cyclers usually stayed longer on the first TNFi (11.4 months vs 14.7 months). Although, switchers had greater severity of psoriasis and worse disease activity at baseline, they seemed to have an increased likelihood of achieving all clinical outcomes compared to cyclers. Even though it did not achieve statistical significance (CIs included 1.0), switchers had 70% greater likelihood of achieving MDA, a nearly 4 times higher likelihood of achieving a SPARCC index score ≤ 1, better improvements in HAQ, global arthritis, pain and morning stiffness scores.

WHY IMPORTANT?

This real-life cohort study results may help clinicians when choosing a 2nd line agent after the 1st line TNFi had failed in PsA patients

POLLING QUESTION

Should having a primary or secondary non-response to TNFi treatment in PsA patients impact your decision on cycling vs switching?

Table 2. Multivariable-adjusted risk ratios (95% CI) estimating the likelihood of achieving clinical outcomes at 6 months follow-up among patients with PsA who switched to another MOA vs cycled to a TNFi from a first line TNFi

Outcome	Adjusted Risk Ratio (95% CI)[a]
Minimal Disease Activity	1.7 (0.9, 3.1)
Tender joint count ≤1	1.1 (0.6, 2.0)
Swollen joint count ≤1	1.3 (0.8, 2.4)
Body surface area ≤3%	1.2 (0.6, 2.6)
Patient pain ≤15	1.3 (0.6, 2.6)
Patient global assessment of arthritis ≤20	1.5 (0.8, 3.0)
Patient global assessment of arthritis MCID (reduction ≥10 points)	1.4 (0.9, 2.0)
HAQ-DI ≤0.5	2.1 (1.0, 4.8)
HAQ-DI MCID (reduction ≥0.35)	1.7 (1.0, 3.0)
SPARCC Enthesitis Index ≤1	3.8 (1.1, 12.8)
Very low disease activity	1.3 (0.5, 3.1)
cDAPSA low disease activity	1.0 (0.4, 2.6)
Morning stiffness MCID (reduction ≥10 points)	1.5 (1.0, 2.3)

Reference group was the cycling treatment group. [a]The model adjusted for race, education, history of anxiety, infections, fibromyalgia and psoriasis, current or prior use of analgesics, current or prior use of NSAIDS, concomitant therapy status, MDA status, and baseline measures of the variable being analyzed, in addition to baseline measures of cDAPSA, BSA, swollen joint count, Physician's Global Assessment of disease activity, Patient's Global Assessment of disease activity, dactylitis, patient-reported pain, stiffness, and % activity impairment. BSA, body surface area; cDAPSA, clinical Disease Activity in Psoriatic Arthritis; CI, confidence interval; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCID, minimal clinically important difference; MDA, minimal disease activity; MOA, mechanism of action; NSAID, nonsteroidal anti-inflammatory drug; SPARCC, Spondyloarthritis Research Consortium of Canada; TNFi, tumor necrosis factor inhibitor.

Prediction of Psoriatic Arthritis Tool (PRESTO): Development and Performance of a New Scoring System for Psoriatic Arthritis Risk

Lihi Eder

ABSTRACT NUMBER: 1612
Oral presentation on
Sunday, November 13
5:15 PM – 5:25 PM

https://acrabstracts.org/abstract/prediction-of-psoriatic-arthritis-tool-presto-development-and-performance-of-a-new-scoring-system-for-psoriatic-arthritis-risk/

The authors aimed to assess the performance of a risk prediction model for the development of PsA among psoriasis patients in 1 and 5-year periods. They retrospectively analyzed the data from a prospective cohort (IPART registry) of psoriasis patients without PsA who were followed from 2006 to 2020. The risk of developing PsA within 1 year was associated with younger age, male sex, family history of psoriasis, back stiffness, nail pitting, level of stiffness, use of biologic medications, global health, and pain severity. Risk factors for developing PsA within 5 years were morning stiffness, psoriatic nail lesion, psoriasis severity (by PASI), fatigue severity (by FACIT-fatigue), pain severity, and use of systemic non-biologic medication or phototherapy. The sensitivity was 54.5% and specificity was 75% for a 2.5% probability of PsA onset within 1 year. The sensitivity and specificity for a 5% probability within 5-years period were 61.1% and 77%. respectively.

WHY IMPORTANT?

Clinicians could use a well-designed prediction tool to identify high-risk Psoriasis patients for developing PsA and thus follow them more closely.

POLLING QUESTION

Do you believe a prediction tool for PsA development in Psoriasis patients is practical and should be used in Dermatology clinics?

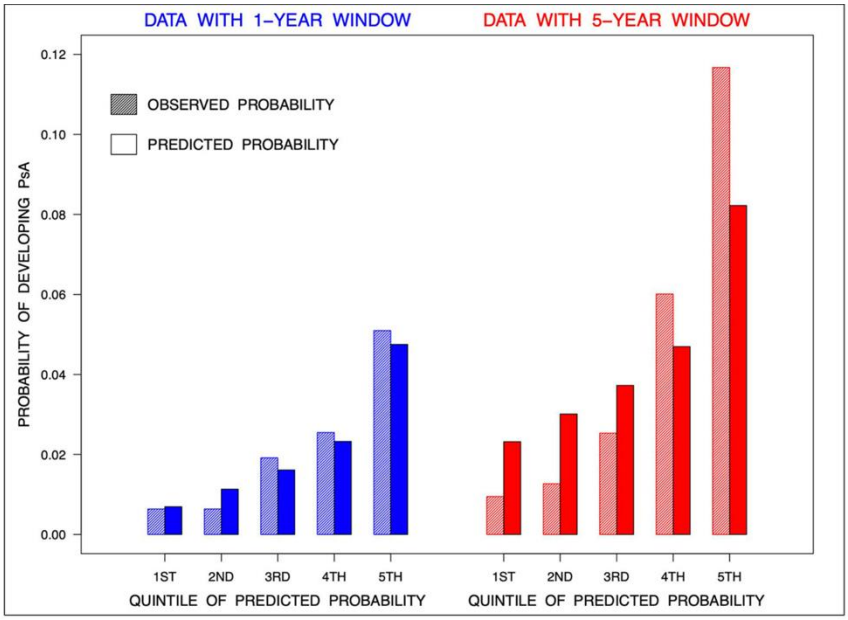


Figure 3: Calibration plots by quintile of predicted vs. observed probabilities for 1-year and 5-year periods

Multimorbidity in Psoriasis as a Risk Factor for Psoriatic Arthritis: A Population-Based Study

Paras Karmacharya

ABSTRACT NUMBER: 1506
Poster presentation on
Sunday, November 13
1:00 PM – 3:00 PM

https://acrabstracts.org/abstract/multimorbidity-in-psoriasis-as-a-risk-factor-for-psoriatic-arthritis-a-population-based-study/

In this population-based incidence cohort of psoriasis who were first diagnosed in 2000-2010, the authors evaluated the association of comorbidities with development of PsA using medical records. Diagnosis codes (≥2 codes at least 30 days apart) within a five-year look-back period were used to determine the presence of comorbidities; ≥1 year of available medical history was required. Comorbidities were defined using 159 categories per modified Clinical Classification Software.

Among 802 patients included to the analysis, 23 patients developed PsA with 14.7 years median follow-up duration. Higher risk of developing PsA was noted with ≥2 comorbidities and ≥5 comorbidities. Comorbidities associated with significantly higher risk of PsA were other nervous system disorders, spondylosis, anxiety, mood disorders, other mental disorders, and fibromyalgia.

WHY IMPORTANT?

To prevent the diagnostic delay in PsA, it is important to screen for comorbidities in psoriasis patients as these could be associated with the development of PsA.

POLLING QUESTION

Do you frequently document and follow-up on comorbidities in your practice, managing PsO/PsA patients?

Neural Networks for Distinguishing Rheumatoid Arthritis from Psoriatic Arthritis by Using Magnetic Resonance Imaging

Lukas Folle

ABSTRACT NUMBER: 1599
Poster presentation on
Saturday, November 12
1:00 PM – 3:00 PM

https://acrabstracts.org/abstract/neural-networks-for-distinguishing-rheumatoid-arthritis-from-psoriatic-arthritis-by-using-magnetic-resonance-imaging/

This study evaluated if it is possible to differentiate seropositive rheumatoid arthritis (RA+), seronegative RA (RA-), and psoriatic arthritis (PsA) using hand MRI data. Neural networks were trained to distinguish (i) RA+ vs. PsA, (ii) RA- vs. PsA and (iii) RA+ vs. RA-. The regions being most important for the neural networks were recorded and correlated to the respective anatomical regions by an experienced rheumatologist. Differentiation between disease entities as measured by the AUROC was 75% (SD 3%) for RA+ vs PsA, 74% (SD 8%) for RA- vs PsA, and 67% (6%) for RA+ vs RA-. Adding demographic and clinical parameters to MR data did not improve the performance of the neural network significantly.
Clinically important regions were also important for the network regions.

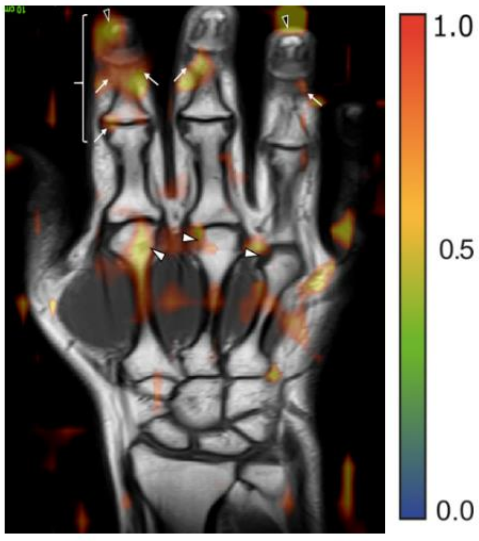
WHY IMPORTANT?

This study suggest that it would be possible to distinguish patients diagnosed with seropositive RA, seronegative RA and PsA by a neural network technique using MRI imaging.

POLLING QUESTION

Do you believe this technique would be helpful in the clinical setting to aid in the diagnosis of inflammatory arthritis?

Figure 2:
MR image with the overlay of the attention map generated by the neural network for a patient affected by PsA. Arrows mark regions of pathological joint changes (soft tissue inflammation and enthesitis).



*André Ribeiro, MD
*Rheumatology Fellow at Hospital de Clínicas de Porto Alegre
*Young Grappa member: Participates in the Education Committee, Do Not Miss, ACR Highlights, and Slide Library Projects

https://www.linkedin.com/in/andre-ribeiro-49b093104

Twitter: dr_AndreRibeiro

Understanding Inter-rater Variability in Scoring of Entheseal Lesions: Results from the Diagnostic Ultrasound Enthesitis Tool (DUET) Study

Lihi Eder

ABSTRACT NUMBER: 2206
Poster presentation on
Monday, November 14
3:00 PM – 4:30 PM

https://acrabstracts.org/abstract/understanding-inter-rater-variability-in-scoring-of-entheseal-lesions-results-from-the-diagnostic-ultrasound-enthesitis-tool-duet-study/

Entheseal activity is a very challenging domain to be assessed in PsA, since it has several possible other etiologies (e.g., chronic overload) and differential diagnosis (e.g., bursitis, fibromyalgia). Therefore, sonographic scoring methods of entheseal lesions are paramount for an accurate diagnosis. The DUET initiative is an international multicenter study that aimed to develop a new scoring system for entheseal activity in PsA. In order to assess for reproducibility, the inter-rater variability was studied: it showed a moderate to substantial agreement for all elementary lesions, being highest for enthesophytes (0.71) and vascularization (0.70), and lowest for thickening (0.43) and calcifications (0.43). Inter-rater agreement was numerically lower for central vs. local readers for most lesions. Most patient characteristics did not have a substantial influence on Kappa statistics, with the exception of obesity, which decreased the Kappa scores for most lesions.

WHY IMPORTANT?

Being able to accurately identify entheseal activity is an essential tool to correctly make a SpA diagnosis.

POLLING QUESTION

How often do you use ultrasound to assess for entheseal activity before considering a change in therapy?

Table 1 – Agreement on scoring of sonographic elementary lesions of enthesitis						
	Prevalence of abnormal lesions (score>0)		Central-central (N=137 patients)		Central-local (N=161 patients)	
	Central*	Local	Raw Agreement	Kappa	Raw Agreement	Kappa
Enthesophyte (0-3)	40%	34%	68.5%	0.71	69.9%	0.71
Vascularization (0-3)	7%	8%	95.2%	0.70	94.1%	0.68
Bursitis (0-2)	19%	24%	83.3%	0.48	80.1%	0.39
Erosion (0-1)	4%	8%	95.9%	0.46	92.8%	0.38
Hypoechogenicity (0-1)	30%	33%	76.5%	0.44	71.3%	0.35
Calcification (0-3)	12%	24%	86.9%	0.43	76.2%	0.29
Thickening (0-1)	19%	28%	82.4%	0.43	74.6%	0.32
***Weighted average among 3 readers**						

TREATMENT

*Ummugulsum Gazel, MD
*Rheumatologist
*Clinical-Research Fellow at University of Ottawa
*Young-GRAPPA member
*Participates in GRAPPA MSUS Working Group
and Imaging Library Project

https://www.researchgate.net/profile/Ummugulsum-Gazel

https://www.linkedin.com/in/ummugulsum-gazel/

Achievement of Different Treatment Targets with Izokibep Demonstrates Efficacy Benefits in Patients with Active Psoriatic Arthritis: Results from a 16-Week Randomized, Placebo-Controlled Phase 2 Clinical Trial

Frank Behrens

ABSTRACT NUMBER: 1597
Oral presentation on
Sunday, November 13
3:00 AM – 3:10 PM

https://acrabstracts.org/abstract/achievement-of-different-treatment-targets-with-izokibep-demonstrates-efficacy-benefits-in-patients-with-active-psoriatic-arthritis-results-from-a-16-week-randomized-placebo-controlled-phase-2-clini/

Izokibep is a unique IL-17A inhibitor: a fusion protein with very high potency, small molecular size, and attachment to albumin. In this multicenter double-blind, placebo-controlled trial, active PsA (≥3 swollen and ≥3 tender joints) patients who had inadequate response to previous treatment (i.e., NSAIDs, csDMARDs, and TNFi) were randomised to either placebo or Izokibep 40 mg or 80 mg subcutaneously Q2W for 16 weeks. The primary end point was ACR50 response at Week 16. Among 135 patients included the study, 13% of placebo, 48% of the 40 mg Q2W group, and 52% of the 80 mg Q2W group (p=0.0006) met the primary endpoint. A clinically meaningful change (≥0.6) in DAS28-CRP between Izokibep treatment groups and placebo was observed as early as 2 weeks. Achievement rate of PASI75 response was also high in both treatment groups. Adverse event rates were similar to placebo and previous IL17 inhibitors.

WHY IMPORTANT?

Izokibep is a new treatment option for multiple disease domains in PsA, including skin and joints, capable of providing an early response.

POLLING QUESTION

Do you believe that being a fusion protein provides a therapeutic advantage for Izokibep?

COI Disclosures: F. Behrens, AbbVie, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Genzyme, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, Bristol-Myers Squibb(BMS), Galapagos, Gilead, UCB, Affibody, MoonLake, GlaxoSmithKlein(GSK); P. Taylor, Biogen, Celltrion, Eli Lilly, Fresenius Kabi, Gilead, GlaxoSmithKlein(GSK), Janssen, Nordic Pharma, Pfizer, Roche, Sanofi, UCB, Galapagos, Abbvie; P. Mease, AbbVie, Amgen, Janssen, Novartis, Pfizer Inc, UCB, Sun Pharma, Eli Lilly, Bristol-Myers Squibb(BMS), Celgene, Genentech; P. Peloso, ACELYRIN, ACELYRIN; D. Wetzel, Affibody; N. Brun, Affibody AB, Affibody AB; B. Wiens, ACELYRIN; J. Brandt-Juergens, AbbVie/Abbott, Bristol-Myers Squibb(BMS), Janssen, Eli Lilly, Merck/MSD, Novartis, Pfizer, Roche, UCB, Sanofi-Aventis, Medac, Gilead, Gilead, Affibody; E. Drescher, None; E. Dokoupilova, None; A. Rowińska-Osuch, None; N. Abdel- Kader Martin, Pfizer; K. de Vlam, UCB, Eli Lilly, Pfizer, AbbVie/Abbott, Merck/MSD, johnson and johnson.

Composite Endpoint	Placebo Q2W	Izokibep 40 mg Q2W	Izokibep 80 mg Q2W	Placebo Q2W	Izokibep 40 mg Q2W *p-value**	Izokibep 80 mg Q2W *p-value**
Number observations	*N=44*	*N=44*	*N=47*	*N=43*	*N=42*	*N=46*
	Week 4 (descriptive)			**Week 16**		
ACR20, % Response	16%	41%	45%	26%	60% *0.0028*	75% *<0.0001*
ACR50, % Response	1%	18%	21%	13%	48% *0.0014*	52% *0.0006*
ACR70, % Response	0%	9%	4%	5%	27% *0.0101*	18% *0.0678*
DAS28-CRP, Mean CFB**	0.19	0.88	0.96	0.64	1.54	1.66
DAPSA, Mean CFB**	4.6	15.4	17.7	13.0	24.8	28.6
MDA, % Response	3%	23%	20%	5%	42% *0.0020*	39% *0.0032*
	Subpopulation with Psoriasis-BSA > 3% at Baseline (74 of 135, 55%)					
Number observations	*N=23*	*N=28*	*N=23*	*N=23*	*N=23*	*N=28*
PASI75, % Response	0%	35%	25%	14%	83%	85%
PASI90, % Response	0%	22%	14%	14%	57%	48%
PASI100, % Response	0%	9%	7%	5%	39%	38%

Full Analysis Set (FAS)
Logistic regression model with fixed factors treatment, visit, treatment by visit interaction, previous TNFi exposure, concomitant csDMARD use, country (pooled), baseline covariate and baseline by visit interaction and random factor subject
* Two-sided p-value derived by using estimated difference between treatments and Placebo at Week 16
** Change from baseline

Efficacy of Guselkumab in Three Cohorts of Biologic-Naïve PsA Patients with Axial Involvement Defined Based on Imaging and Machine-Learning Criteria: Pooled Analysis of Two Phase 3 Studies

Philip Mease

ABSTRACT NUMBER: 1035
Poster presentation on
Sunday, November 13
9:00 AM – 10:30 AM

https://acrabstracts.org/abstract/efficacy-of-guselkumab-in-three-cohorts-of-biologic-naive-psa-patients-with-axial-involvement-defined-based-on-imaging-and-machine-learning-criteria-pooled-analysis-of-two-phase-3-studies/

This study analysed the efficacy of Guselkumab (GUS) in axial PsA (axPsA) in a cluster cohort of Discover 1 and 2 studies. The post-hoc analysis included only bio-naïve patients who met the definition of axPsA: imaging-confirmed sacroiliitis, machine learning identification, or both. At week 8, regardless of AxPsA definition, GUS treatment was associated with significant improvements in BASDAI, mBASDAI, spinal pain, morning stiffness, and ASDAS. These results were enhanced through W24. Finally, the study also showed positive results regarding the proportion of patients who reached the categorical BASDAI & ASDAS endpoint at W24.

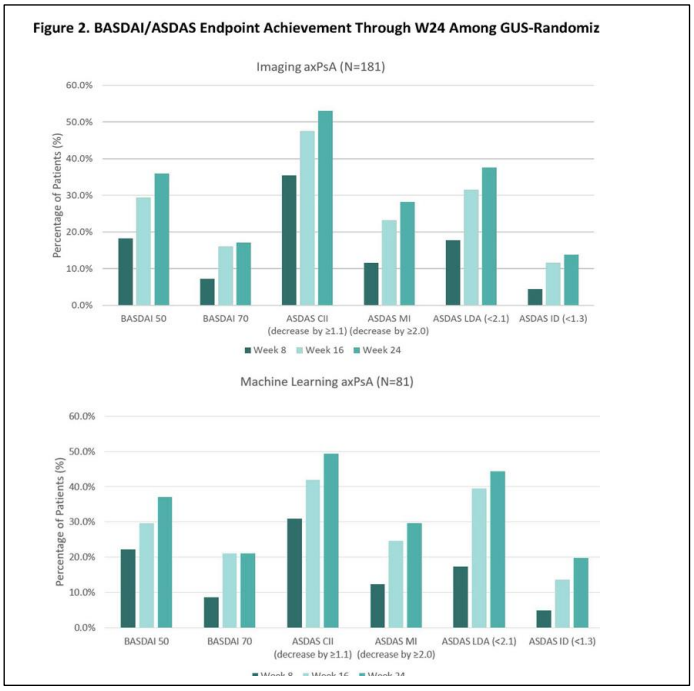
WHY IMPORTANT?

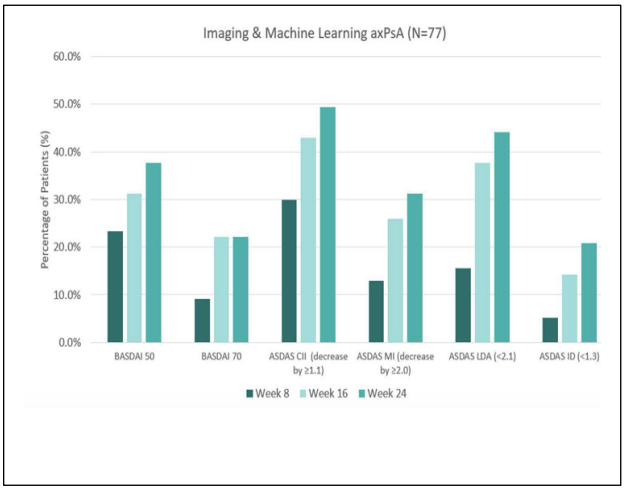
Currently, the absence of a unified definition of axPsA makes it challenging to study this pathology. This study showed that GUS is a new option in axPsA defined by imaging and/or machine learning criteria.

POLLING QUESTION

Does this study results influence your treatment decision in PsA patients who have both peripheral and axial involvement?

COI Disclosures: P. Mease, AbbVie, Amgen, Janssen, Novartis, Pfizer Inc, UCB, Sun Pharma, Eli Lilly, Bristol-Myers Squibb(BMS), Celgene, Genentech; W. Tillett, AbbVie, Amgen, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB; S. Ohrndorf, AbbVie, Pfizer, Bristol-Myers Squibb(BMS), Janssen, Novartis, Amgen, Roche, Mylan (Viatris Company); M. Perate, Janssen Pharmaceutical Companies of Johnson and Johnson; M. Medysky, Janssen Scientific Affairs, LLC, Johnson & Johnson; M. Zimmermann, Janssen Scientific Affairs, LLC, Johnson & Johnson; M. Shawi, Janssen Pharmaceutical Companies of Johnson and Johnson; E. Rampakakis, Janssen, JSS Medical Research; P. Bird, AbbVie/Abbott, Eli Lilly, Gilead, Janssen, Merck/MSD, Pfizer, UCB, Novartis; A. Zabotti, AbbVie, Amgen, Janssen, Eli Lilly, Novartis, UCB; A. Deodhar, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer Inc, UCB Pharma, Aurinia, Moonlake; D. Gladman, AbbVie, Amgen, Eli Lilly, Janssen, Gilead, Novartis, Pfizer, Bristol-Myers Squibb(BMS), Galapagos, UCB Pharma, Celgene.





Safety and Efficacy of Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 Inhibitor, in Patients with Psoriatic Arthritis: 52-Week Results from a Randomized Phase 2 Trial

Philip Mease

ABSTRACT NUMBER:1598
Oral presentation on
Sunday, November 13
3:30 PM – 3:40 PM

https://acrabstracts.org/abstract/safety-and-efficacy-of-deucravacitinib-an-oral-selective-tyrosine-kinase-2-inhibitor-in-patients-with-psoriatic-arthritis-52-week-results-from-a-randomized-phase-2-trial/

The results of a previous placebo-controlled, phase 2 trial, studied the efficacy of Deucravacitinib (DEUC) in PsA at week 16 (Part A). This new study (Part B) assessed the continuous safety and efficacy of DEUC up to 52 weeks. Patients receiving DEUC who had achieved MDA at week 16 (Part A) continued DEUC treatment, and those who had not were switched to Ustekinumab (UST). In Part A, 25% of DEUC patients achieved MDA at week 16 and continued the drug; all other patients were switched to UST in Part B: PBO, 100%; DEUC 6 mg QD, 78%; DEUC 12 mg QD, 72%. Decreases in mean PASDAS score as well as improvements in other clinical and patient-reported outcomes observed at week 16 were maintained at week 52, with no new safety signals observed.

WHY IMPORTANT?

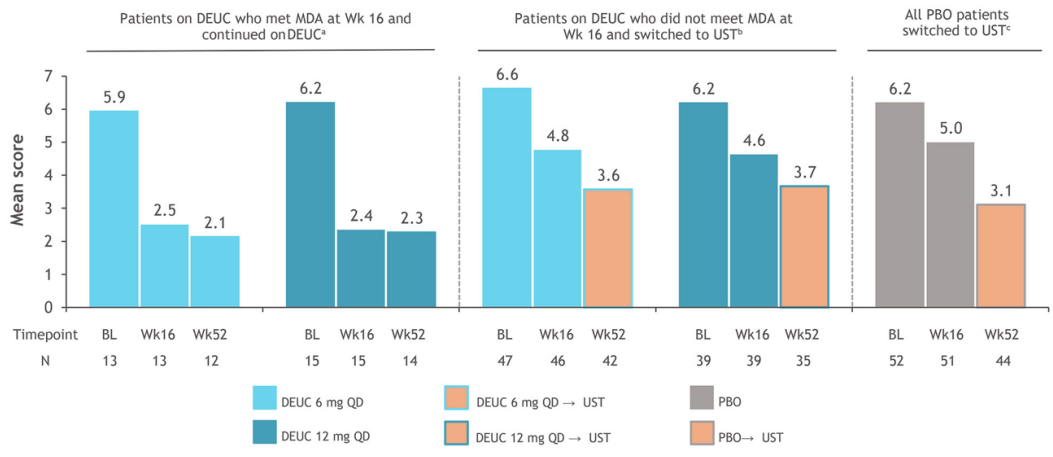
DEUC was more efficacious than placebo up to 16 weeks, and maintained its efficacy and safety up to 52 weeks of treatment.

POLLING QUESTION

Do you believe that DEUC is an effective treatment for the majority of the disease domains in PsA, considering this study used PASDAS as an efficacy endpoint?

COI Disclosures: P. Mease, AbbVie, Amgen, Janssen, Novartis, Pfizer Inc, UCB, Sun Pharma, Eli Lilly, Bristol-Myers Squibb(BMS), Celgene, Genentech; A. Deodhar, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer Inc, UCB Pharma, Aurinia, Moonlake; D. van der Heijde, AbbVie, Bayer, BMS, Cyxone, Eisai, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Novartis, Pfizer, UCB, Imaging Rheumatology bv, Lilly; F. Behrens, AbbVie, Pfizer, Roche, Amgen, Chugai, Prophylix, Novartis, Boehringer, UCB, Bristol Myers Squibb, Celgene, MSD, Biotest, Janssen, Genzyme, Lilly, Sandoz, Sanofi; A. Kivitz, Amgen, Boehringer-Ingelheim, Janssen, Gilead, GlaxoSmithKlein (GSK), Novartis, Pfizer, Sanofi, Flexion, Eli Lilly, Genentech, UCB, AbbVie, Merck, ECOR1 CAPITAL, LLC, Chemocentryx, Regenerson, Grunenthal, Bendcare, Horizon; J. Neal, AbbVie, Amgen, Eli Lilly, Genentech, Novartis, UCB, Pfizer, Gilead, Bristol Myers Squibb; M. Nys, Bristol Myers Squibb; T. Lehman, Bristol Myers Squibb; N. Delev, Bristol-Myers Squibb(BMS); S. Korish, Bristol Myers Squibb; M. Nowak, Bristol Myers Squibb; S. Banerjee, Bristol Myers Squibb

Figure. Mean PASDAS score through Week 52



[a]Interpretation of data limited by small sample size. [b]Interpretation of data limited by different patient populations. [c]All patients treated with PBO in Part A switched to UST at Wk 16, regardless of MDA status; 5 patients had achieved MDA at Wk 16. All data are as observed.
BL, baseline; DEUC, deucravacitinib; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; QD, once daily; UST, ustekinumab; Wk, week.

Bimekizumab Treatment in Patients with Active Psoriatic Arthritis and Inadequate Response to Tumor Necrosis Factor Inhibitors: 16-Week Efficacy and Safety from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study

Joseph Merola

ABSTRACT NUMBER: 1599
Oral presentation on
Sunday, November 13
3:30 PM – 3:40 PM

https://acrabstracts.org/abstract/bimekizumab-treatment-in-patients-with-active-psoriatic-arthritis-

BE COMPLETE is a 16-week, double-blinded, placebo-controlled study of Bimekizumab (BKZ), a selectively inhibitor of IL-17F and IL-17A, in PsA patients who were TNFi resistant. Patients were eligible if they had ≥3 tender and swollen joints, ≥1 active psoriatic lesion and/or documented history of psoriasis, and inadequate response or intolerance to 1–2 prior TNFi. The primary endpoint was ≥50% improvement in ACR50 response criteria at Week 16. Among 388 patients, 43% patients in the BKZ arm and 6.8% in the PBO arm reached the primary end point. Similarly, BKZ has been showed to be effective on skin disease (assessed with PASI) compared to PBO. Regarding the tolerability, BKZ showed efficacy without new safety signals.

WHY IMPORTANT?

Bimekizumab may be an alternative treatment option in TNFi-resistant PsA patients, with an acceptable safety profile.

POLLING QUESTION

Would you consider Bimekizumab as an option in TNFi resistant PsA patients after viewing these results?

COI Disclosures: J. Merola, AbbVie, Biogen, BMS, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, UCB Pharma, Arena, Avotres, EMD, LEO Pharma, Merck, Regeneron, Sanofi; R. Landewé, Abbott, Amgen, AstraZeneca, BMS, GSK, Novartis, Merck, Pfizer, Schering-Plough, UCB Pharma; I. McInnes, Bristol-Myers Squibb (BMS), Janssen, Novartis, UCB, Pfizer, AbbVie, Celgene, AstraZeneca, Boehringer Ingelheim, EveloBio, LEO, Lilly; P. Mease, AbbVie, Amgen, Janssen, Novartis, Pfizer Inc, UCB, Sun Pharma, Eli Lilly, Bristol-Myers Squibb(BMS), Celgene, Genentech; C. Ritchlin, UCB, AbbVie, Eli Lilly, Pfizer Inc, Novartis, Janssen, Bristol-Myers Squibb; Y. Tanaka, Lilly, AbbVie, Bristol Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Pfizer, Mitsubishi Tanabe, GlaxoSmithKline, Asahi Kasei, Takeda, Astellas, Janssen, Novartis, Sanofi, UCB, YL Biologics, MSD, Ono, Taisho Toyama, Celltrion, Gilead, Boehringer-Ingelheim, Corrona, Kowa, Amgen, AstraZeneca, AstraZeneca, Eli Lilly; A. Asahina, AbbVie, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Pharma, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, UCB Pharma, Celgene; F. Behrens, AbbVie, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Genzyme, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, Bristol-Myers Squibb(BMS), Galapagos, Gilead, UCB, Affibody, MoonLake, GlaxoSmithKlein(GSK); D. Gladman, AbbVie, Amgen, Eli Lilly, Janssen, Gilead, Novartis, Pfizer, Bristol-Myers Squibb(BMS), Galapagos, UCB Pharma, Celgene; L. Gossec, Amgen, Lilly, Pfizer, Sandoz, UCB Pharma, AbbVie, Bristol Myers Squibb, Gilead, Janssen, Novartis, Samsung Bioepis, Sanofi-Aventis, Galapagos, GlaxoSmithKlein (GSK), Celltrion, MSD; R. Warren, AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, UCB Pharma, DiCE, Union; B. Ink, UCB Pharma, GlaxoSmithKlein(GSK); D. Assudani, UCB Pharma; R. Bajracharya, UCB Pharma; J. Coarse, UCB Pharma; L. Coates, AbbVie, Amgen, Boehringer-Ingelheim, Bristol-Myers Squibb (BMS), Eli Lilly, Gilead, Galapagos, Janssen, Medac, Novartis, Pfizer, UCB, Celgene, Biogen, Moonlake, GlaxoSmithKlein (GSK).

Table. Efficacy endpoints at Week 16

	Endpoint	PBO (N=133)	BKZ 160 mg Q4W (N=267)	p value
Ranked endpoints	ACR50* [NRI], n (%)	9 (6.8)	116 (43.4)	<0.001
	HAQ-DI CfB† [RBMI], mean (SE)	–0.1 (0.0)	–0.4 (0.0)	<0.001
	PASI90†,[a] [NRI], n (%)	6 (6.8)[b]	121 (68.8)[c]	<0.001
	SF-36 PCS CfB† [RBMI], mean (SE)	1.4 (0.7)	7.3 (0.5)	<0.001
	MDA† [NRI], n (%)	8 (6.0)	118 (44.2)	<0.001
Other endpoints	ACR20† [NRI], n (%)	21 (15.8)	179 (67.0)	-
	ACR70† [NRI], n (%)	1 (0.8)	71 (26.6)	-
	PASI75[a] [NRI], n (%)	9 (10.2)[b]	145 (82.4)[c]	-
	PASI100[a] [NRI], n (%)	4 (4.5)[b]	103 (58.5)[c]	-
	ACR50+PASI100[a] [NRI], n (%)	1 (1.1)[b]	59 (33.5)[c]	-
	mNAPSI CfB[d] [MI], mean (SE)	–0.4 (0.2)[e]	–2.7 (0.2)[f]	-
	TJC CfB [MI], mean (SE)	–2.4 (0.9)	–10.9 (0.8)	-
	SJC CfB [MI], mean (SE)	–2.0 (0.5)	–7.0 (0.4)	-

Randomized set. P values are only presented for pre-specified, multiplicity-adjusted and powered analyses. *Primary endpoint; †Secondary endpoint. [a]In patients with ≥3% BSA with PSO at BL; [b]n=88; [c]n=176; [d]In patients with mNAPSI >0 at baseline; [e]n=83; [f]n=159. ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; BKZ: bimekizumab; BSA: body surface area; CfB: change from baseline; HAQ-DI: Health Assessment Questionnaire Disability Index; MI: multiple imputation; mNAPSI: modified Nail Psoriasis Severity Index; NRI: non-responder imputation; PASI75/90/100: ≥75/90/100% improvement in the Psoriasis Area and Severity Index; PBO: placebo; PSO: psoriasis; Q4W; every 4 weeks; RBMI: Reference Based Multiple Imputation; SE: standard error; SF-36 PCS: Short-Form 36-Item Health Survey Physical Component Summary; SJC: swollen joint count; TJC: tender joint count.

*André Ribeiro, MD
*Rheumatology Fellow at Hospital de Clínicas de Porto Alegre
*Young Grappa member: Participates in the Education Committee, Do Not Miss, ACR Highlights, and Slide Library Projects

https://www.linkedin.com/in/andre-ribeiro-49b093104

Twitter: dr_AndreRibeiro

Bimekizumab Treatment in Biologic DMARD-Naïve Patients with Active Psoriatic Arthritis: 52-Week Efficacy and Safety Results from a Phase 3, Randomized, Placebo-Controlled, Active Reference Study

Christopher Ritchlin

ABSTRACT NUMBER: L02
Late-breaking abstract
Monday, November 14
9:00 AM – 10:30 AM

https://acrabstracts.org/abstract/bimekizumab-treatment-in-biologic-dmard-naive-patients-with-active-psoriatic-arthritis-52-week-efficacy-and-safety-results-from-a-phase-3-randomized-placebo-controlled-active-reference-study/

The phase 3 study BE OPTIMAL demonstrated superiority of bimekizumab (BKZ) over placebo (PBO) in joints and skin at week 16. BE OPTIMAL enrolled bDMARD naïve patients who had active PsA and compared it to PBO and adalimumab (ADA). Patients in the placebo group were switched to BKZ 160 mg Q4W at week 16. The efficacy and safety over 52 weeks are presented here; At week 52, ACR50 was achieved at 53.0% PBO/BKZ, 54.5% BKZ, 50.0% ADA. Complete skin clearance was achieved by 65.0% PBO/BKZ, 60.8% BKZ, 48.5% ADA. Finally, MDA was achieved by 53.7% PBO/BKZ, 55.0% BKZ, 52.9% ADA. Radiographic progression was minimal in all groups. BKZ was well tolerated, with no new safety signals observed; Candida infections were reported in 7.7% of BKZ patients (vs. 0.7% ADA), with all cases being mild/moderate, and only 1 case of oral candidiasis leading to discontinuation of the drug.

WHY IMPORTANT?

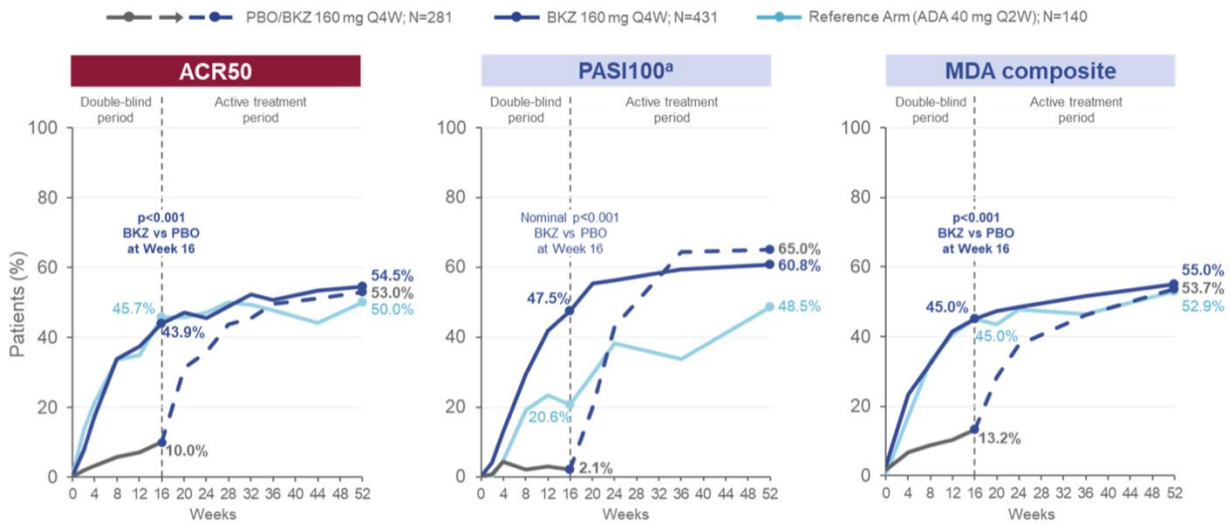
This 52-week efficacy and safety study of BKZ shows that the drug maintains its efficacy over time without adding new safety concerns about cancer and MACE.

POLLING QUESTION

Do you consider starting an IL-17 inhibitors instead of a TNFi in biologic naïve patients with more severe skin disease?

COI Disclosures: C. Ritchlin, AbbVie, Amgen, UCB Pharma, Eli Lilly, Gilead, Janssen, Novartis, Pfizer; L. Coates, AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, UCB Pharma, Bristol-Myers Squibb(BMS), Boehringer Ingelheim, Domain, Galapagos, Moonlake, GlaxoSmithKlein(GSK), Medac; I. McInnes, AbbVie, AstraZeneca, Bristol-Myers Squibb(BMS), Boehringer Ingelheim, Cabaletta, Causeway Therapeutics, Celgene, Eli Lilly, Evelo, Janssen, Moonlake, Novartis, UCB Pharma; P. Mease, AbbVie, Amgen, Bristol-Myers Squibb(BMS), Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, UCB Pharma, Acelyrin, Aclaris, Boehringer Ingelheim, Galapagos, GlaxoSmithKlein(GSK), Moonlake; J. Merola, AbbVie, Amgen, Bayer, Bristol-Myers Squibb(BMS), Dermavant, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma; Y. Tanaka, AstraZeneca, AbbVie, Bristol-Myers Squibb(BMS), Boehringer Ingelheim, Chugai, Daiichi-Sankyo, Eisai, Lilly, Gilead, GlaxoSmithKlein(GSK), Mitsubishi Tanabe, Pfizer, Asahi-Kasei, Takeda; A. Asahina, AbbVie, Amgen, Bristol-Myers Squibb(BMS), Boehringer Ingelheim, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, UCB Pharma; L. Gossec, Amgen, Eli Lilly, Galapagos, Pfizer, Sandoz, UCB Pharma, AbbVie, Bristol-Myers Squibb(BMS), Celltrion, Gilead, GlaxoSmithKlein(GSK), Janssen, Novartis; A. Gottlieb, Amgen, AnaptysBio, Avotres Therapeutics, Bristol-Myers Squibb(BMS), Boehringer Ingelheim, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, XBiotech, Ortho Dermatologics; D. Thaci, AbbVie, Almirall, Amgen, Biogen, Bristol-Myers Squibb(BMS), Celltrion, Eli Lilly, Galapagos, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB Pharma; B. Ink, UCB Pharma, AbbVie, GlaxoSmithKlein(GSK); D. Assudani, UCB Pharma; R. Bajracharya, UCB Pharma; V. Shende, UCB Pharma; J. Coarse, UCB Pharma; R. Landewé, AbbVie, AstraZeneca, Bristol-Myers Squibb(BMS), Eli Lilly, Novartis, Pfizer, UCB Pharma, Rheumatology Consultancy BV

Figure 1. ACR50, PASI100, and MDA composite responders to Week 52 [NRI]



Randomized set. Primary endpoint: ACR50 at Week 16. ACR50 measured at Weeks 2, 4, Q4W to Week 36, and Weeks 44 and 52; PASI100 at Weeks 2, 4, Q4W to Week 24, and Weeks 36 and 52; MDA at Week 4, Q4W to Week 24, and Weeks 36 and 52. [a]In patients with psoriasis affecting ≥3% BSA at baseline; PBO/BKZ 160 mg Q4W: N=140; BKZ 160 mg Q4W: N=217; ADA 40 mg Q2W: N=68. ACR: American College of Rheumatology; ADA: adalimumab; BKZ: bimekizumab; MDA: minimal disease activity; NRI: non-responder imputation; PASI: Psoriasis Area and Severity Index; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.