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2023

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

ANNUAL MEETING NEWSLETTER

DUBLIN IRELAND, JULY 13-15, 2023

- **PROJECT UPDATES**
  Get the updates on the latest GRAPPA research projects.
- **TRAINEE SYMPOSIUM**
  47 abstracts submitted from 13 countries. Read on to learn more.
- **PILOT RESEARCH GRANTS**
  Read about the 4 new recipients of the 2023 Pilot Research Grants.
- **AND MORE!**
  Other topics include Young GRAPPA, workshops, debates, election results, and more!

LARGEST REGISTRATION TO DATE

286 in-person registrants & 328 virtual from over 36 countries.

GRAPPA CELEBRATES 20 YEARS

20 YEAR ANNIVERSARY

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

WELCOME

MESSAGE FROM GRAPPA'S CO-PRESIDENTS

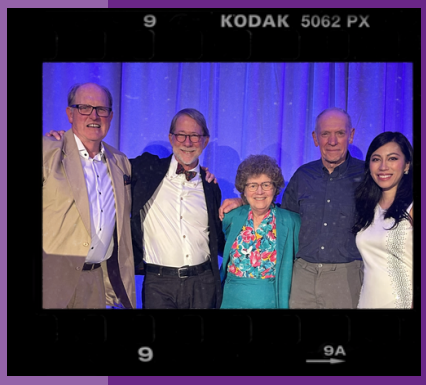
Our GRAPPA annual meeting in Dublin, July 2023, was hugely successful. As we celebrate our 20th anniversary, we are pleased to see GRAPPA growing from strength to strength. We hope that you enjoy reading about the progress that continues to be made in this evolving landscape. You can also view all presentations on demand on the GRAPPA website.

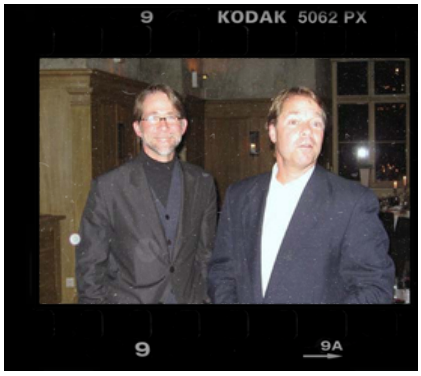
We would like to thank all who have worked hard to put together this newsletter. In particular, we thank our Y-GRAPPiAns for their substantial contributions to this newsletter and for being a vibrant cohort in our GRAPPA community.

GRAPPA Co-Presidents
April Armstrong and Oliver FitzGerald

GRAPPA IS CELEBRATING 20 YEARS!

Watch 20th Anniversary Video





Three of GRAPPA's founding members, **Dr. Philip Helliwell (UK), Dr. Philip Mease (US) and Dr. Dafna Gladman (Canada),** gave a speed tour of the history and achievements of GRAPPA:

In the late 1990s and early 2000s there were only a few PsA centers worldwide, but the advent of the first biologics kick started world-wide activity in PsA. The CASPAR group, set up to develop new classification criteria for PsA, included global centers and inspired by ASAS, expanded into GRAPPA. The founders were clear that dermatologists as well as rheumatologists should be integral from the beginning. Today, GRAPPA has more than 1,000 members from 65 countries worldwide, and members also include radiologists, geneticists, methodologists, epidemiologists, patient research partners, and biopharmaceutical industry representatives.

The first GRAPPA meeting was held in August 2003 in a blacked-out New York City. The aim of establishing GRAPPA was to increase awareness and early diagnosis of psoriasis and PsA; the development and validation of research assessment tools to measure clinical status and disease outcome; the evaluation of treatment modalities and treatment recommendations; supporting and conducting basic research on disease pathophysiology; fostering communication between rheumatologists, dermatologists, representatives of patient advocacy organizations, biopharmaceutical companies, regulatory agencies, and others who are interested in the advancement of care of psoriasis and PsA.

Over the years, GRAPPA has had numerous successes. Important projects and achievements include:

- CASPAR
- GRAPPA-OMERACT project on outcome measures in PsA
- GRACE project
- Treatment recommendations: 2009, 2015, 2022
- Education
  - Combined dermatology/rheumatology meetings
  - Slide library
  - The GRAPPA app
  - Training videos
- GRAPPA-industry projects
- Collaborative Research Network (CRN, now Research Committee)
  - Innovative Medicines Initiative (IMI) consortium HIPPOCRATES
  - Accelerating Medicines Partnership (AMP) – autoimmune and immune-mediated diseases: ELLIPSS consortium
- AXIS – GRAPPA ASAS collaboration

Moreover, Young-GRAPPA was founded in 2021 with the aim of supporting young clinicians and early career researchers.

GRAPPA Membership in 2023

63 Countries

MEMBER TYPE	NORTH AMERICA	NON NORTH AMERICA	TOTAL
Dermatologist	108	176	284
Rheumatologist	160	494	654
Geneticist	5	3	8
Methodologist	2	11	13
Radiologist	2	3	5
Other/Scientist	20	42	62
GRAPPA PRP	3	7	10
TOTAL	300	736	1,036

EARLY CAREER MEMBERS	FULL GRAPPA MEMBERS	TOTAL
153	883	1,036

REFLECTING ON GRAPPA

Philip Helliwell

What is your best GRAPPA memory? “Many, many great memories but the best I think would be the AM in Naples several years ago where several ‘famous old timers’ turned out on the dance floor to music made by GRAPPiAns.”
What have you gotten out of GRAPPA? “The satisfaction that we have made significant advances in psoriatic disease.”
Which has been GRAPPA’s biggest achievement? “Too many to list but treatment recommendations and OMERACT must rank high, and bringing people together from across the globe.”
How do you see GRAPPA evolving in the next 20 years? “That’s up to you Y-GRAPPiAns I think!”

Dafna Gladman

What is your best GRAPPA memory? “Best memory is the first meeting in New York. There was a feeling of novelty, comradery, and participation. The meeting achieved a lot in a very short time.”
What have you gotten out of GRAPPA? “Mainly friends around the world. Opportunity to discuss topics related to psoriatic disease among people interested in the condition.”
Which has been GRAPPA’s biggest achievement? “There are quite a few – starting with determining outcomes in clinical trials, treatment recommendations, establishing the research net, Y-GRAPPA.”
How do you see GRAPPA evolving in the next 20 years? “It is up to the younger generation to evolve GRAPPA. I see it continuing to grow, develop closer ties among researchers, further develop treatment recommendations, identify biomarkers for susceptibility, disease activity and damage.”

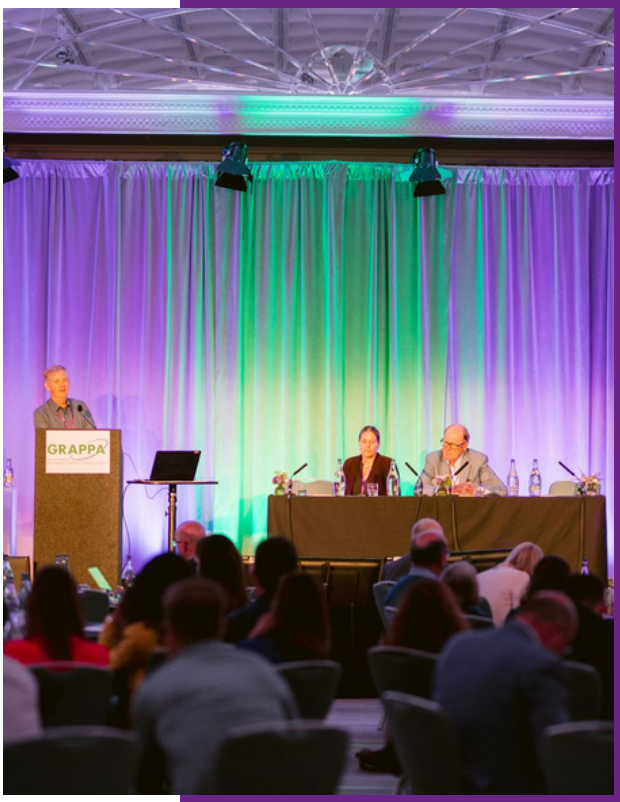
Philip Mease

What is your best GRAPPA memory? “One unforgettable memory was the post-dinner dance party at a GRAPPA annual meeting in Naples, Italy, when John Moll of the historical Moll&Wright PsA criteria that preceded CASPAR, was dancing with both my wife, Laura Kastner, and Philip Helliwell’s wife, Maggie Helliwell, while the GRAPPA “band”, Heya, led by Valderilio Acevedo of Brazil, played Beatles tunes.”
What have you gotten out of GRAPPA? “Too many things to enumerate and describe! The GRAPPA members around the world represent a wonderful community of friendship, intelligent discourse, thoughtful, knowledgeable and caring clinicians, productive and creative researchers to collaborate with, and dynamic educators of other clinicians and patients. GRAPPA has provided me with a productive platform for research, education, and the opportunity to mentor younger clinicians coming along.”
Which has been GRAPPA’s biggest achievement? “Provision of a society that brings together clinicians and patient research partners, old and young, from around the world, to collaborate on research and education about psoriatic disease.”
How do you see GRAPPA evolving in the next 20 years? “I believe it will continue to grow, continue to conduct cutting edge research and provide education around the world, and inspire young clinician researchers and educators to come into the field of psoriatic disease.”

PATIENT RESEARCH PARTNERS

Patient research partners (PRPs) are persons with a psoriatic disease who join a research team as equal partners to share knowledge from their lived experience but also speak on behalf of all patients. GRAPPA PRPs **Dr. Suzanne Grieb, US, and Dr. Maarten de Wit, The Netherlands,** spoke about the involvement of PRPs in GRAPPA research:

- PRP involvement in research aligns with focus on patient-centered care; it increases the relevance of research to patient priorities and needs.
- PRPs contribute throughout the research process, from pre-conception and study design to study conduct, analysis, and dissemination.
- GRAPPA has a ten-year history of PRP involvement in research; this involvement is still growing and may have different forms.
- Inclusion of PRPs as equal partners is still challenging, for example:
  - Researchers have difficulty delegating and sharing responsibility.
  - Communication: Medical and research language is difficult to understand for PRPs; they require lay summaries and dedicated time for training and explanation.
  - Achieving diversity, inclusivity and representativity requires extra effort in terms of time, energy, and resources.
  - Lack of knowing how to build effective partnerships in basic and translation research.



PRP CHAIR'S MESSAGE

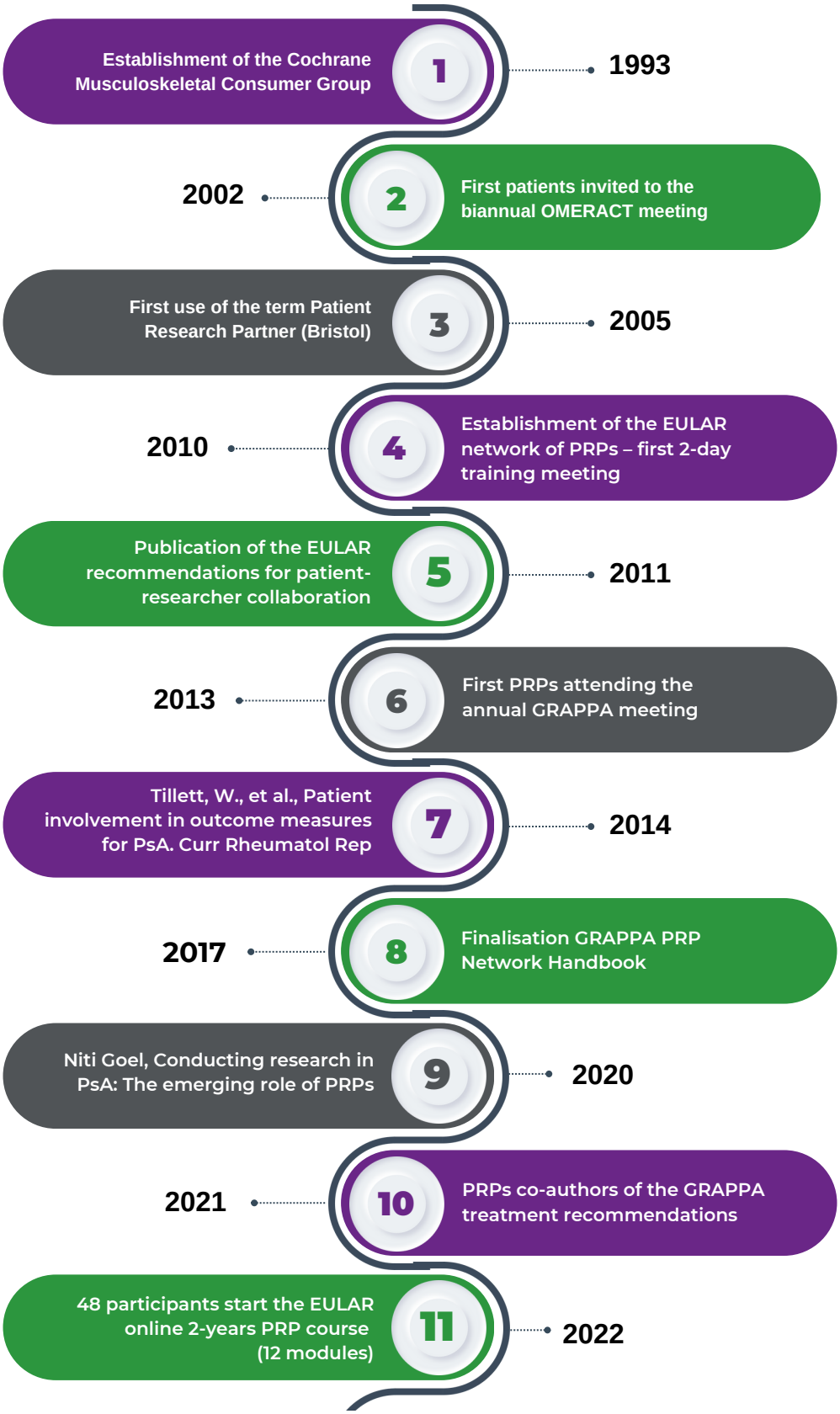
The GRAPPA (PRP) network continues its contribution to GRAPPA missions with increased involvement in various activities. Their Chair, **Arnon Katz, Israel,** summarizes their work:

In addition to existing collaborations within GRAPPA and other patient groups, the PRPs participate in new activities. These include the slide library project, the research committee, educational initiatives, HIPPOCRATES projects, and growing contributions to publications.

Looking forward, we will build a comprehensive and representative PRP section on the new GRAPPA website. We shall expand involvement in different activities, and grow the PRP team, which currently includes twelve dedicated patient members with various backgrounds and careers, from seven countries. The increased request for PRP involvement in a growing number of activities, combined with the need for diversification of the PRP group, requires the recruitment of patients from various backgrounds and origins. The Board of Directors supports this approach. We are currently formatting recruitment guidelines and processes.

We emphasize the importance of reflecting and representing the patient voice and support the physicians, researchers, and scientists of the greater GRAPPA community in numerous GRAPPA projects and studies. And finally, we shall continue to develop a close working relationship with Y-GRAPPA.

MILESTONES
OF PATIENT INVOLVEMENT IN RHEUMATOLOGY RESEARCH



PROJECT UPDATES

AXIS STUDY

The AXIS study is a joint ASAS-GRAPPA initiative which aims to define axial PsA. The study recruits consecutive patients diagnosed with PsA with symptom duration <10 years and not receiving b- or tsDMARDs. Their clinical and imaging data are reviewed by central clinical and imaging review committees.

Dr. Dafna Gladman, Canada, presented on the progress of AXIS: There are now 57 participating centers in 21 countries, and recruitment has started in 16 countries. By the end of June, 294 out of the anticipated 400 patients had been included. Of these, the eCRF was complete for 233 patients, and central clinical and imaging review complete for 123 and 171 patients respectively.

AXIAL PSA MOLECULAR AND CLINICAL CHARACTERIZATION STUDY

The Axial PsA Molecular and Clinical Characterization Study is the first study to be conducted by GRAPPA CRN and **Dr. Philip Mease, US,** presented the study design and progress. The hypothesis is that there are liquid and/or tissue biomarkers associated with the presence of axial PsA.

The study anticipates enrolling 40 participants with PsA: 20 patients with and 20 patients without axial involvement. All participants will meet CASPAR criteria, have active disease, be within 10 years of PsA diagnosis and naive to b- and tsDMARDs. They will be assessed at baseline with a clinical assessment, imaging (plain X-ray and MRI), and tissue samples. All participants will provide blood and stool samples, 80% will have skin biopsies taken and 50% will undergo synovial biopsy. Detailed molecular analysis will be performed on the tissue samples.

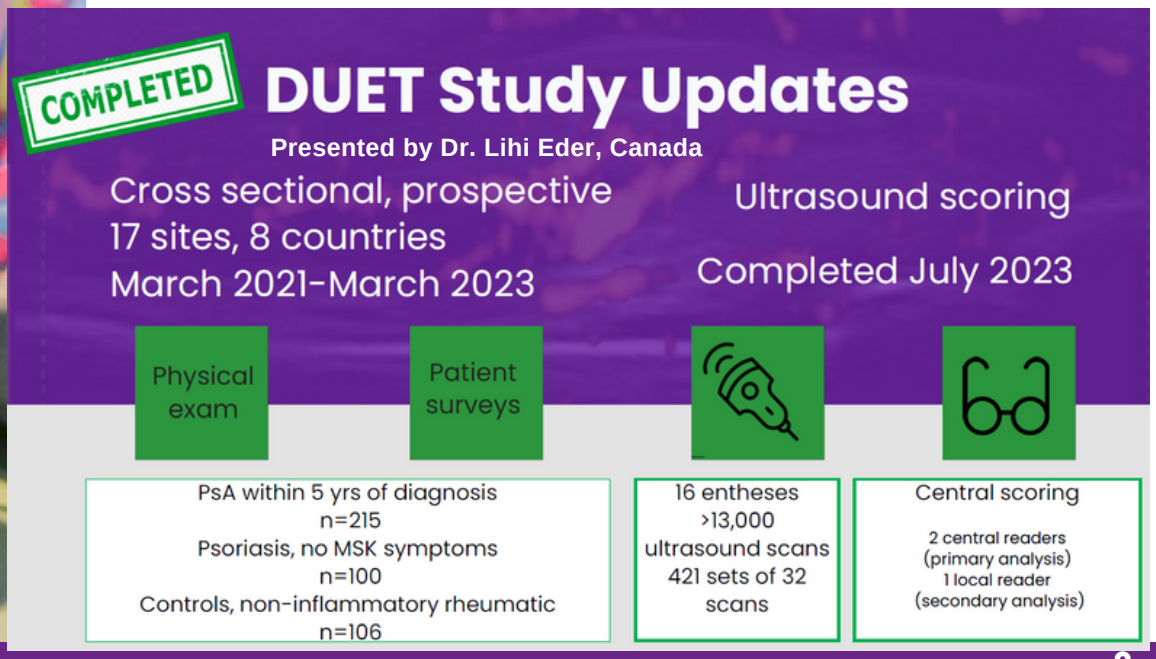
There are 9 recruitment sites in 7 countries, and the 5 first participants have been recruited in Seattle, US. This study is funded by Janssen.

The aim of HIPPOCRATES is to significantly improve the outcomes of patients with PsA. It will do this through 8 interconnected work packages that embed and involve patients, clinicians, regulators, and pharmaceutical company partners.

Dr. Oliver Fitzgerald, Ireland, gave an update on the progress of HIPPOCRATES which includes:

-Establishing well-functioning work packages and cross working group teams.
-A pilot multi-omics analysis of the BioCOM cohort (University College Dublin).
-A consortium-wide material transfer agreement and data sharing agreement to support the sharing and analysis of additional prioritized cohorts.
-Multiple conference abstracts (posters and presentations) and peer-reviewed publications.
-The launch of the HIPPOCRATES prospective observational study (HPOS), coordinated by Laura Coates (Oxford).

HPOS aims to recruit 25,000 individuals with psoriasis across Europe and monitor for progression to PsA with a view to identifying predictors of progression. The study is all online and participants can register on the website - please spread the word!



TREATMENT SATISFACTION

DermSat-7 is a 7-item psoriasis treatment satisfaction tool that covers the domains of effectiveness of treatment and convenience of use. **Dr. April Armstrong, US**, presented data on a study in which her team at University of Southern California and the teams at Brigham and Women's and Mount Sinai enrolled 142 participants to test the DermSat-7. Participants completed the DermSat-7 questionnaire on Day 1 and Day 14 of starting a new treatment.

Preliminary analysis found the DermSat-7 to have construct validity and known-groups validity when compared with validated instruments (TSQM-9, PASI, PGA, DLQI). Further analysis will determine internal consistency and test-retest reliability.

The next steps are to:
- adapt the DermSat-7 questionnaire to reflect the experience of patients with both psoriasis and PsA.
- recruit participants to a longitudinal validation study of DermSat-11 which includes the additional domain of adverse events.

TREATMENT RECOMMENDATIONS

Dr. Laura Coates, UK, provided an update on Treatment Recommendations:

- The 2021 recommendations have been translated into Portuguese and Spanish and can be accessed here.
- Work on the next Treatment Recommendations will start in the next 1-2 years.

Meanwhile, feedback on the process is welcome via the GRAPPA website.

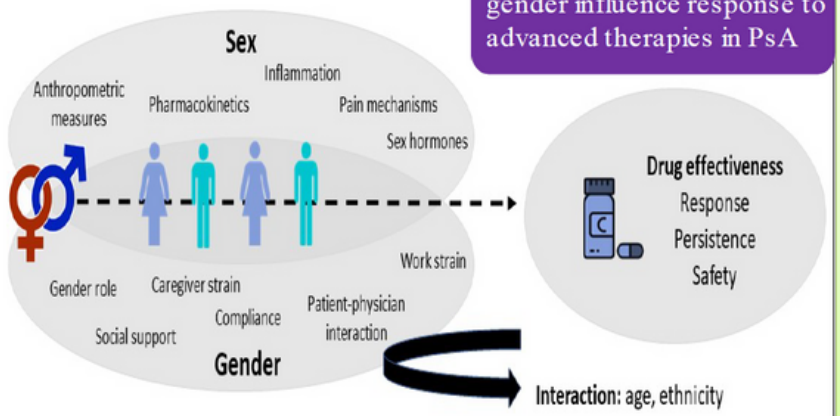
SAGE-PsA Update

Presented by Dr. Lihi Eder, Canada

SAGE-PsA

OBJECTIVE

Understand how sex and gender influence response to advanced therapies in PsA



- 121 GRAPPA members applied for participation
- 36 SAGE-PsA participating sites were selected
- 19 study surveys translated into 12 languages
- 1st patient enrolled in January 2023 (Toronto)
- Kick-off meeting: March 2023
- 10 patients enrolled
- 6/36 active sites
- 15/36 sites signed the contract

OMERACT AND VAS UPDATE

Dr. Ying-Ying (Katy) Leung, Singapore, presented an update of the composite measure for PsA project:

- The purposes of candidate composite measures for PsA were defined in 2022.
- GRAPPA stakeholders rated MDA as critically important, while ACR20/50/70, DAPSA, PASDAS, CPDAI and 3 and 4 VAS were rated as important for appraisal using the OMERACT filter. A systematic literature review is in progress.

The GRAPPA 2019 workshop identified the 3 and 4 VAS (Figure) as composite PsA disease measurements which may be feasible to use in routine clinical care. **Dr. William Tillett, UK,** presented work demonstrating:

- The ability of the 3 and 4 VAS to discriminate between placebo and treatment arms from the DISCOVER, COSMOS and SELECT clinical trial datasets and good discrimination in the DEPAR observational dataset in early PsA. There were strong correlations with other clinical and health-related quality of life (HRQoL) outcome measures in the same datasets.
- Numeric rating scale versions also discriminate and correlate with clinical and HRQoL outcomes.
- External estimates for thresholds of meaning and minimal clinically important difference.
- Achievement of 3 VAS LDA or 4 VAS REM is associated with less structural damage.

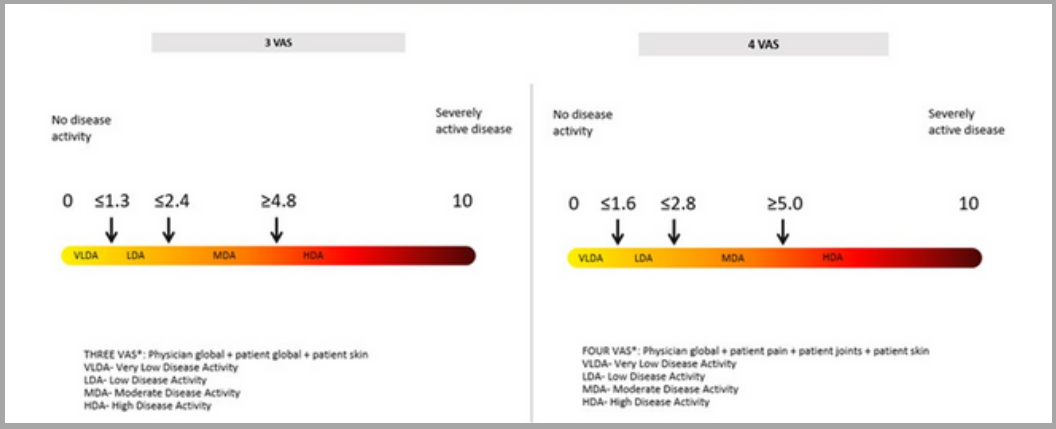


FIGURE: 3 AND 4 VAS

SLIDES LIBRARY

The new GRAPPA Slides Library has been released!

With the aim of widespread use for educational purposes, the slide decks created in 2013 have been updated by a great team of senior and Y-GRAPPA members. The GRAPPA Education Committee co-ordinated the project with the supervision and co-ordination of **Dr. Philip Helliwell (UK), Dr. Fabian Proft (Germany) and Dr. Gizem Ayan (Turkey).** Valuable logistical support was provided by **Janine Kowack and Annie Spangler.**

All slides are available in English and can be accessed by anyone. You can find slides by searching by keywords, or by browsing one of the categories: Genetics; Pathogenesis & Tissues; Classification, Epidemiology & Prognosis; Clinical Features; Imaging; Psoriatic Skin Disease; Psoriatic Nail Disease; Psoriasis Treatment; Psoriatic Arthritis Treatment; Outcome Measures.

Stay tuned for the next step which will be the translation of the deck into different languages!

SCAN ME!

IDEOM MSK-Q

The IDEOM MSK-Q is a patient-reported questionnaire developed by IDEOM to capture the intensity and impact of musculoskeletal symptoms on quality of life in patients who have psoriasis with or without PsA. **Dr. Joseph Merola, US, and Dr. Perez-Chada, US,** presented its background and progress.

The development of the IDEOM MSK-Q included multiple rounds of pilot testing involving patients with psoriatic disease and health-care professionals to ensure the content validity of the instrument. Additionally, a ratification exercise conducted in accordance with the OMERACT filter for approving core outcome measure instruments confirmed the instrument's match with target domain (truth) and feasibility. Utilizing data from a cross-sectional survey of a random sample of 1453 individuals with psoriasis distributed by the National Psoriasis Foundation, the structural, convergent, and known-groups validity of the instrument were further confirmed.

The IDEOM MSK-Q is currently being used in Phase III/IV clinical trials, the Cohort for Psoriasis and Psoriatic Arthritis Registry (COPPAR), the Preventing Arthritis in a Multi-Center Psoriasis At-Risk Cohort (PAMPA) trial, and the Psorcast Hybrid Study. Future studies will assess its cross-cultural validity, responsiveness, and adaptation for use in other conditions such as hidradenitis suppurative and pustular psoriasis.

BREAKOUT SESSION

10 breakout Groups With 3 Questions

Report Back by **Dr. Sam Hwang, US** and **Dr. Cláudia Goldenstein Schainberg, Brazil**

Q1: WHAT ARE CURRENT CHALLENGES OF DERM/RHEUM COLLABORATION IN YOUR REGION?

Resource Limitations:

- Scarcity of dermatologists and rheumatologists, coupled with constraints on time and cost.
- Challenges in communication and relationship-building between the two specialties.

Accessibility and Structural Challenges:

- Disparities in urban vs rural areas and across different countries.
- Long waiting times, different locations of specialists, and physical infrastructure limitations.

Financial Constraints:

- Absence of funding for combined clinics and specific dermatologist appointment payments.

Telemedicine and Diagnosis:

- Challenges in assessing joints and diagnosing PsA virtually.

Educational Gaps:

- Limited interest and expertise in PsA among dermatologists.
- Need for integrated training, brief educational materials, and improved MSK examination skills.

Q2: WHAT HAVE YOU SEEN ARE THE INNOVATIVE METHODS OF ENCOURAGING COLLABORATION?

Global Perspective & Tailored Strategies:

- Recognize unique needs across countries and emphasize tailored collaboration methods.

Education & Virtual Collaboration:

- Enhance disease knowledge and educate stakeholders through online meetings, social media, and virtual interdisciplinary sessions.

Telemedicine In-Person Approaches:

- Telemedicine for follow-ups while emphasizing the importance of in-person consultations, especially for first-time visits.

Technological & Role Integration:

- Employ ”extended role practitioners” for specialized triage.
- Incorporate ultrasound imaging, AI for symptom screening, apps for patient data, and electronic questionnaires.

Industry Engagement:

- Collaborate with industry for funding and support in driving innovative collaboration methods.

Q3: HOW DO WE IDENTIFY THOSE AT HIGH RISK FOR DEVELOPING PSA AMONG PSORIASIS PATIENTS – HOW SHOULD WE SCREEN AND REFER?

Diagnostic Challenges:

- Recognizing early-PsA is difficult due to limited data and heterogeneity. Aim for a balance to avoid under or over-diagnosis.

Awareness, Education, and Outreach:

- Raise awareness among patients with psoriasis and educate other medical specialties.
- For broader outreach, use educational videos, telemedicine, and telecasting during prime hours.

Patient Engagement:

- Promote patient self-referral, association involvement, and public information campaigns.

Technological Integration:

- Utilize apps, AI, and wearable tech for early screening and diagnosis.
- Integrate AI with precision medicine for targeted identification.

Collaboration, Tools, and Funding:

- Foster Derm/Rheum collaborations and multidisciplinary approaches.
- Develop advanced screening tools and engage the industry to fund innovative projects.

NEW PROJECTS

EPIDEMIOLOGY

With many exciting opportunities for becoming engaged with projects in GRAPPA there has been discussion on whether there is a demand for some “taster” sessions in research methods and specifically epidemiology.

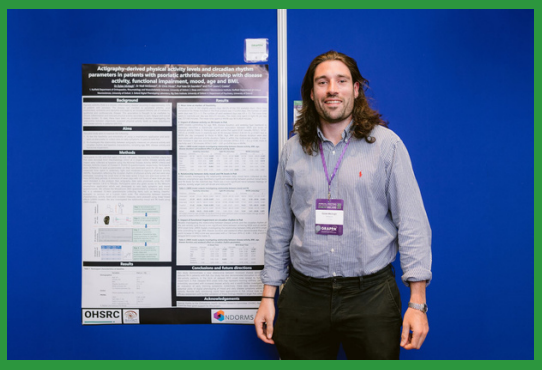
Dr. Gary Macfarlane, UK, presented a survey of GRAPPA members to gauge interest: Over 90 members responded and 89% indicated an interest in attending training in epidemiology methods. Most of the respondents identified as being at mid or late career stage but we hope the courses offered might be specifically of interest to those in Y-GRAPPA.

The plan is to organize a primer session on the day before the first full day of GRAPPA 2024 and to cover topics such as Study Design; Analysis; Methodological Issues and Key Skills. Watch out for more information.

COMPARISON OF A PHYSICIAN-BASED VERSUS QUESTIONNAIRE-BASED APPROACH TO IDENTIFY PATIENTS WITH A HIGH PROBABILITY OF PSORIATIC ARTHRITIS AMONG PATIENTS WITH PSORIASIS: A PROSPECTIVE MULTICENTER STUDY (COMPOSITION)

The COMPOSITION study aims to improve the early diagnosis of PsA by evaluating the performance of a physician-based screening and referral strategy compared to a patient-based questionnaire. **Dr. Denis Poddubbny, Germany,** presented the study strategy which involves two steps: completing the PEST questionnaire and undergoing a musculoskeletal evaluation by a dermatologist.

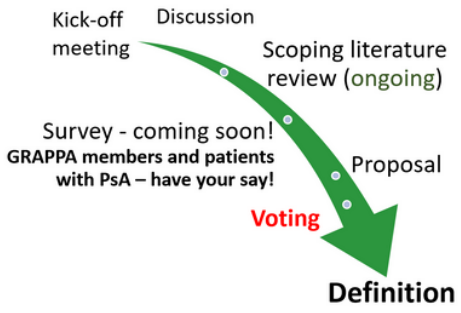
-Patients meeting referral criteria (PEST or Physician-positives; a double negative control group is also planned) will be referred to a rheumatologist for further evaluation.
-The study will assess the proportion of patients diagnosed with PsA using the new strategy compared to the questionnaire alone.
-Around 500 patients with psoriasis will be included, and evaluated by pairs of dermatology and rheumatology centers to improve diagnostic accuracy and patient care.
-GRAPPA members will be contacted and asked for active contribution.



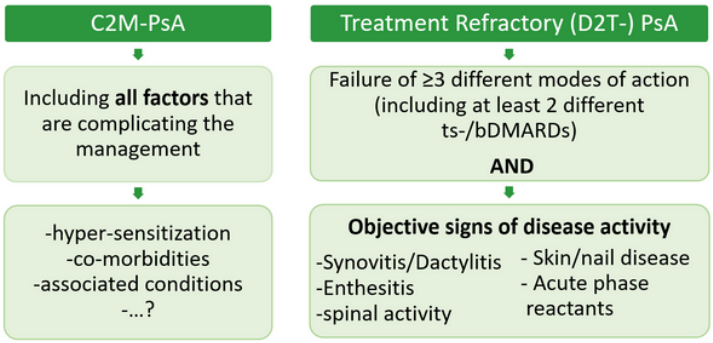
GRAPPA Research Project: Definition of Difficult-to-Treat (D2T-) / Complex-to-Manage (C2M-) PsA

- As treatment options expand, it's crucial to ***define those individuals not adequately responding to the available treatment options***. Through characterizing these patients, we will deepen our understanding of the pathophysiology, and pave the way for the development of new treatment strategies and modes of action.
- The working group is comprised of rheumatology and dermatology GRAPPA members, 2 Y-GRAPPiAns and ≥1 patient research partner.
- **Dr Fabian Proft, Germany,** encouraged involvement of the wider GRAPPA membership at the survey and voting stages!

Project Outline



Initial Proposal to Start the Discussion



D2T UK Pilot

Since February 2022, **Dr. Deepak Jadon, UK,** has chaired an online videoconference every two months for clinicians in the East of England, UK, serving a population of 6.3 million people and including 8 government hospitals. He presented his experiences from the review panel which discusses complex difficult-to-treat patients with peripheral and axial spondyloarthritis:

This study will be beneficial to:

• Patients:
- Consolidation of the current management plan and reassurance that treatment options are not missed.
- Sanctioning to use novel approaches, e.g. combining advanced therapies.

• Health care workers: Very educational experience for all and camaraderie.

• The Institution:
- Reduced referrals, urgent referrals, medicine costs, recruitment to clinical trials with access to novel treatments.
- Harmonization of care.

Practical tips

• Brief referral proforma to summarize past treatments and focus mind on question(s) being asked.
• Written MDT outcome note and prospective collection of outcome data.
• Video-conference meetings.
• Improve logistics, but F2F better when possible.
• Screen-sharing for images.
• Conscious of online security.

The review panel is, however, not a substitute for meeting the patients yourself and examining them!

DIFFICULT TO MANAGE - PATIENT PERSPECTIVE

Patients often view their diseases differently than their health care professional (HCP), mostly because it can impact them in so many ways that are not apparent at a visit or check in. **Chris Lindsay, US,** provided four points which may help HCPs explore meaningful questions to understand the patient's perspective:

● Efficacy: Is the medication or treatment plan working? How many therapies or how much time has elapsed before the patient feels they are difficult to treat? For some it may be two as they expected new therapies to work right away and for others it might be 6 or more.

● Impact: Are the therapies working across all domains of disease? Is it realistic to find a therapy(ies) that work across all domains? For example, enthesitis and swollen or painful joints.

● Values: We all need to understand and discuss what patients value most and their goals for treatment. This may impact willingness to consider alternatives and helps us listen to and consider alternate plans of care (shared decision making).

● Partnership: Patients and HCPs alike should always have a plan in case new therapies don't work – what options are up for consideration one step down the road?

TRAINEE SYMPOSIUM

47 abstracts submitted

12 reviewers

97.5 Highest Score

5 Oral

21 Posters

13 Countries Submitted Abstracts

- UK - 10
- USA - 8
- Brazil - 6
- Argentina -4
- Canada - 3
- China - 3
- Italy - 3
- Netherlands - 3
- Germany - 2
- Turkey - 2
- Israel - 1
- Pakistan - 1
- Taiwan- 1

ORAL PRESENTERS

Ruchi Shah, US: Regulatory role of JAK signaling on keratinocytes and synovial cells: Novel mechanisms for JAK inhibitors in psoriatic disease

Specific T cells in psoriatic disease lead to inflammation through cytokines like IL-9 and IL-22 which signal through JAK/STAT pathways and are known to act on T cells.
This study explored the effects of IL-9 and IL-22 on keratinocytes and fibroblast-like synoviocytes (FLS) from patients with psoriasis and PsA.

Cultured FLS and keratinocytes were treated with rIL-9 and rIL-22, with and without the JAK-1 inhibitor upadacitinib, and their proliferation and JAK/STAT protein phosphorylation were studied.

Both cytokines induced proliferation of FLS, and this was reduced by upadacitinib.
In keratinocytes, rIL-22 induced proliferation also. Upadacitinib inhibited keratinocyte proliferation and reduced JAK/STAT phosphorylation.

These data show that IL-9, IL-22 and upadacitinib act at the level of FLS and keratinocytes, thus demonstrating a novel mechanism of JAK-1 inhibitors in psoriatic disease.

Courtney Carroll, US: Genome-Guided Proteomic Analysis Identified Biomarkers for the Progression from Psoriasis to PsA

Biomarkers for the progression from psoriasis to PsA would aid the early diagnosis of PsA and enable patients to start DMARD treatment early, before irreversible joint damage has occurred. This study analyzed samples from the Utah Psoriasis Initiative (Salt Lake City, USA).

Whole exome sequencing analysis identified one gene (OSTF1) and two gene sets (Cobalamin Binding and Osteoclast Differentiation) associated with PsA, yielding 6 candidate biomarkers.

Plasma protein levels of two candidate biomarkers (TCN1 and OSTF1) were down-regulated before conversion to PsA; plasma protein levels of one candidate biomarker (TRAP) were up-regulated before conversion to PsA.

TCN1 and TRAP conferred additional predictive value beyond that of clinical features for predicting PsA among patients with cutaneous-only psoriasis.

THANK YOU TO THE REVIEWERS!

Lucy Durham, UK: Single cell sequencing reveals shared CD8+ T cell clones between skin and synovial tissue in PsA

This study used single cell RNA sequencing to compare CD8+ T-cells from paired samples of inflamed skin epidermis, synovial tissue and blood from patients with PsA.

Type-17 CD8+ tissue resident memory (TRM) cells were enriched in both the skin and the joint compared to the blood.

Inflamed skin contained a higher proportion of CD8+ TRM cells and a stronger IL-17 signature compared to the joint. In contrast, granzyme K expressing TRM were enriched in the joint compared to the skin.

Investigation of the T-cell receptor in the skin and the joint identified CD8+ T-cells of the same clonotype that were shared between both sites and the shared clones had similar phenotypes in both sites.

These data indicate that the T-cell infiltrate in skin and synovium is linked and suggest the possibility that T cells migrate between the skin and the joint.

James Sullivan, US: Exploring Pharmacogenetic Variants for Predicting Response to Anti-TNFα Therapy in Patients with PsA

In a cohort of 161 patients with PsA, TNF receptor 2 single nucleotide polymorphism rs1061622 status was associated with nonresponse to anti-TNFα therapy.

Nonresponse was defined as discontinuation of the medication for reason other than insurance, cost, or adverse effect.

Multivariable logistic regression model adjusting for age at PsA diagnosis, sex, and BMI found that patient who had at least 1 G allele of rs1061622 were 5 times more likely to be anti-TNFα therapy non-responders.

These results support the possible role for pharmacogenomic profiling in predicting treatment response among patients with PsA. The mechanism of nonresponse warrants further investigation and is currently in progress.

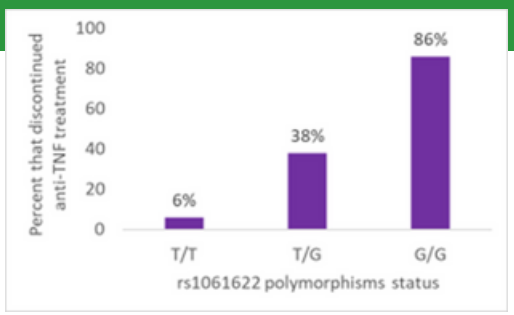


Figure: Unadjusted results from 161-person cohort

Omar Alzayat, US: TRPM4 promotes psoriasiform dermatitis and is a potential therapeutic target for psoriasis

- Gain of function mutations in the TRPM4 calcium activated non-selective cation channel cause progressive symmetric erythrokeratoderma, a genetic syndrome that occurs in infants and young children. The clinical features are similar to human psoriasis.
- TRPM4 gain-of-function (GoF) mice show exaggerated psoriasiform dermatitis upon imiquimod application and western diet feeding.
- TRPM4 GoF increases keratinocyte proliferation and enhances dendritic cell migration, and the TRPM4 inhibitors Glibenclamide and “Compound 5” reduce bone marrow dendritic cell migration.
- The next step is to test TRPM4 inhibitors in vitro and in vivo with the aim of developing effective therapeutics for psoriasiform dermatitis.

DEPRESSION AND ANXIETY IN PSORIASIS AND PSORIATIC ARTHRITIS

Presented by Dr. Elizabeth Wallace, US

1. Patients with psoriasis and PsA are at an increased risk of developing depression and anxiety. Patients with psoriasis with more severe disease and younger age may be at a greater risk for suicide.

2. Certain proinflammatory cytokines have been proposed to contribute to the development of both psoriasis and depression.

3. Clinicians should be aware of this association, inform patients of the mental health comorbidities in psoriatic disease, and have a referral plan for patients who need mental health care. One screening tool that can be implemented in a busy clinic to screen for depression is the Patient Health Questionnaire (PHQ)-2.

4. There are certain treatment considerations that should be factored into an individualized treatment plan in patients with psoriatic disease with a history of depression .

DEPRESSION AND ANXIETY - PATIENT PERSPECTIVE

Depression, anxiety, and mood disorders are complicated. Inflammation can drive depression and vice versa. The overall impact is multidimensional, and there is still a lot of work to be done to understand the interplay between inflammatory disease and mood.

These disorders impact people with psoriatic disease in a multitude of ways: effectiveness of care, response to treatment, remission rates, and of course, quality of life. However, mood disorders can be assessed and treated effectively.

As patients, we are not asking our rheumatologist or dermatologist to be a therapist or prescribe medications for mood disorders, explained **Chris Lindsay, US,** presenting on behalf of **Niti Goel, US**. We are, however, asking that this topic be discussed with us at our visits related to our psoriatic disease and that the HCPs understand that anxiety and depression may be a result of the disease still being active and/or impact our outcomes. There should be a care team partner or referral HCP who understands how to screen/diagnose and treat anxiety and depression. So please consider building a plan within your institution or office setting to address mood disorders in the patient population to allow them to get the care they need for these issues. This ultimately will help your patients achieve better outcomes and potentially change the trajectory of your patients' treatment responses.

PILOT RESEARCH GRANTS

Predicting response to treatment in those receiving biologic therapy in PsA: linking clinical, imaging and molecular markers to better stratify patients

The presence of enthesitis in PsA may provide clues to disease pathogenesis, aid diagnosis, and be a poor prognostic indicator. Ultrasound is an invaluable tool in assessing entheseal disease. **Dr. Ashley Elliott, UK,** presented his work which aimed to better understand enthesitis in PsA and its response to different classes of biologic treatments by integrating clinical assessment, imaging, and proteomic analysis.

His study compared the effect of TNF inhibition (TNFi) and IL17 inhibition (secukinumab) on US-confirmed enthesitis in PsA for the first time. Over 16 weeks of treatment in a biologic naive cohort of 80 patients, there was an overall reduction in enthesitis scoring with biologic treatments. The was a larger reduction in active entheseal disease in patients treated with TNFi versus secukinumab. This merits further exploration.

Proteomic analysis of serum samples identified a panel of 35 candidate biomarkers related to enthesitis on imaging. Future work will include verification of these findings in a larger independent dataset. The possibilities of linking clinical, imaging, and laboratory analysis are vital to address unmet needs in psoriatic disease and provide precise, personalised care for our patients.

Unravelling the effect of HLA-B27 on gut microbial/metabolic profile in PsA

PsA affects about 30% of people with psoriasis. It is associated with the risk gene HLA-B27, which is present in almost 50% of patients with PsA. **Dr. Tejpal Gill, US,** and colleagues have previously shown that HLA-B27 alters the gut microbiota in healthy individuals.

Preliminary results from her current study revealed a decrease in the fecal microbial diversity in patients with PsA in comparison to healthy controls. However, this decrease was not affected by HLA-B27. Since gut microbial function is redundant, she further analyzed the fecal metabolic profile. Interestingly, many inflammatory fecal metabolites were increased in patients with PsA and the differences were more pronounced in HLA-B27 negative patients.

Taken together, the results from this study have the potential to identify HLA-B27 associated microbial and metabolic markers.

The Role of Mechanotransduction in Hyperactivation of TFGβ Via αVβ6 Integrin in Psoriatic Epidermis

Mechanical stress is a well-established trigger for psoriasis, but the underlying molecular mechanism is poorly understood. TGFβ is a pro-inflammatory cytokine implicated in psoriasis pathogenesis. Latent TGFβ needs to be activated through its latency-associated peptide (LAP). Integrins are a class of mechanosensitive receptors, and αVβ6 integrin can bind to LAP and activate TGFβ. **Dr. Maria Shutova, Switzerland,** presented her project which investigates how mechanical forces activates TGFβ during skin inflammation:

-Keratinocytes express αVβ6 and αVβ6 is upregulated in psoriatic skin.
-A cocktail of cytokines (IL-17A, IL-22, OSM, IL-1α, TNFα) induces the expression of αVβ6 in epidermal cultures, with increased αVβ6-dependent surface binding of LAP.
-Keratinocytes display mechanodependent LAP binding.

These initial data suggest that increased TFGβ signalling in psoriasis is due to:
-Latent TFGβ overexpression
-Increased αVβ6 surface expression on keratinocytes
-Increased αVβ6 dependent mechanical activation of TFGβ

2023 RECIPIENTS

$25,000 PILOT RESEARCH GRANT

CLINICAL SCIENCE

AXEL SVEDBOM

Mentor: Mona Ståhle

Karolinska University Hospital and the Karolinska Institutet Sweden

Prediction of Psoriatic Arthritis in New Onset Psoriasis

TRANSLATIONAL SCIENCE

STEVEN DANG

Mentor: Lihi Eder

University of Toronto Canada

Sex differences in serum proteomic biomarkers in psoriatic arthritis

BASIC SCIENCE

OMAR ALZAYAT

Mentor: Samuel Hwang

UC Davis School of Medicine, USA

TRPM4 Function in Western Diet Induced Psoriasis via IL-23 Mediated Inflammation

$35,000 PILOT RESEARCH GRANT

TRANSLATIONAL SCIENCE

CAROLINE GROSS

Mentors: Michaela Koehm, Frank Behrens, and Andreas Pinter

University Hospital Frankfurt/Main & Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Germany

Immunological maps to guide phenotyping of psoriasis patients at different risk levels to develop psoriatic arthritis by integration of clinical, molecular (multi-OMICs) and innovative imaging assessment using NIR-fluorescence optical imaging technique as indicator for changes in vascularization as preliminary marker for inflammatory processes in psoriatic arthritis

THANK YOU TO THE PILOT RESEARCH GRANT REVIEWERS

Comparative Single-Cell Genomic Profiling of Synovial Fluid Versus Skin Lesions in Psoriatic Arthritis

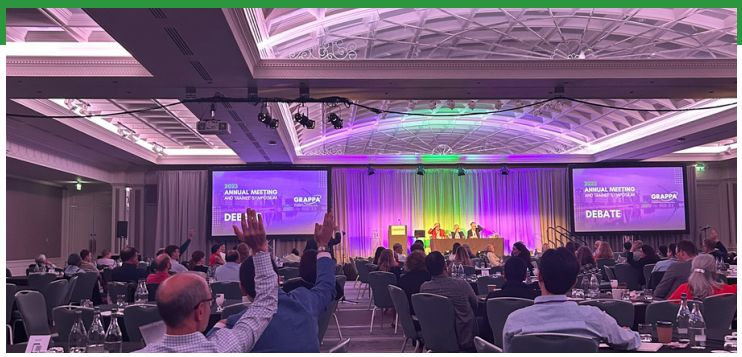
IL-17A inhibitors are highly effective in treating psoriasis but not as effective in treating PsA. **Dr. Jaehwan Kim, US,** used single-cell genomic profiling to explore the role of the IL-17/IL-23 pathway in psoriatic disease pathogenesis by:

1) Characterizing immune cell changes in psoriasis skin lesions before and after IL-17A blockade.
2) Comparing gene expression in psoriasis lesions to PsA synovial fluid immune cells.

IL-17A inhibition brings immune cells and keratinocytes in psoriatic lesions closer to a healthy state. Notably, IL-17A, IL-17F, and IL-23 receptors were upregulated in CD161+ T-cells before treatment but returned to “healthy” levels post-blockade. Similarly, IL-23A in semi-mature dendritic cells, and DEFB4B, DEFB4A, and IL-36G in keratinocytes were upregulated before treatment and normalized after IL-17A inhibition.

Compared to skin lesions, there were more mononuclear phagocytes, plasma cells and B cells in PsA synovial fluid, and the expression of immunoglobulin genes was increased. Moreover, IFN pathway induced genes were enriched in PsA synovial fluid.

These findings underscore differential immune responses in the skin and joint compartments in psoriatic disease. Future work will explore differences in T-cell subsets.



BIOLOGICS FOR MILD PSORIASIS: A POINT-COUNTERPOINT DISCUSSION

This session showcased the controversies of using biologics for mild psoriasis. **Dr. Alice Gottlieb, US,** presented reasons for using biologics for mild psoriasis, and **Dr. Brian Kirby, Ireland,** presented reasons against, mainly starting with the perspective that patients with limited body surface area is defined empirically as 3% or <5% body surface area (BSA).

Arguments for:

- Patients with limited BSA often have PsA and should not be considered “mild” and justify biologic use for both skin and joint disease.
- Similarly, special sites (e.g. face, scalp, palmoplantar, inverse/genital) are associated with significant impact on QoL; some biologics have efficacy data for special sites.
- The International Psoriasis Council reclassification study supports these points in redefining mild psoriasis.
- There are data suggesting that patients with psoriasis treated with biologics may have a lower risk for developing PsA.

Arguments against:

- Many national and society guidelines, including GRAPPA, have recommended that patients with limited disease should start with topical therapy, and agrees that patients with special sites, those with significant impact on QoL, or those with PsA requiring systemic agents should not be categorized as mild.
- New topicals (tapinarof, roflumilast) further expand our options for mild psoriasis.
- The body of work examining risk of PsA in patients treated with biologics does not convincingly support using biologics for mild psoriasis to prevent PsA citing bias, design flaws, and conflicting data.
- Risk of serious infection (1.4-1.5 cases/100 patient-years) and cost of therapy (including monitoring and screening) do not justify biologics in truly mild psoriasis.

In the discussion, additional points were made regarding disease severity from regulatory and research perspectives, how biologics may alter the phenotype.

DEBATE: ENTHESITIS THEORY

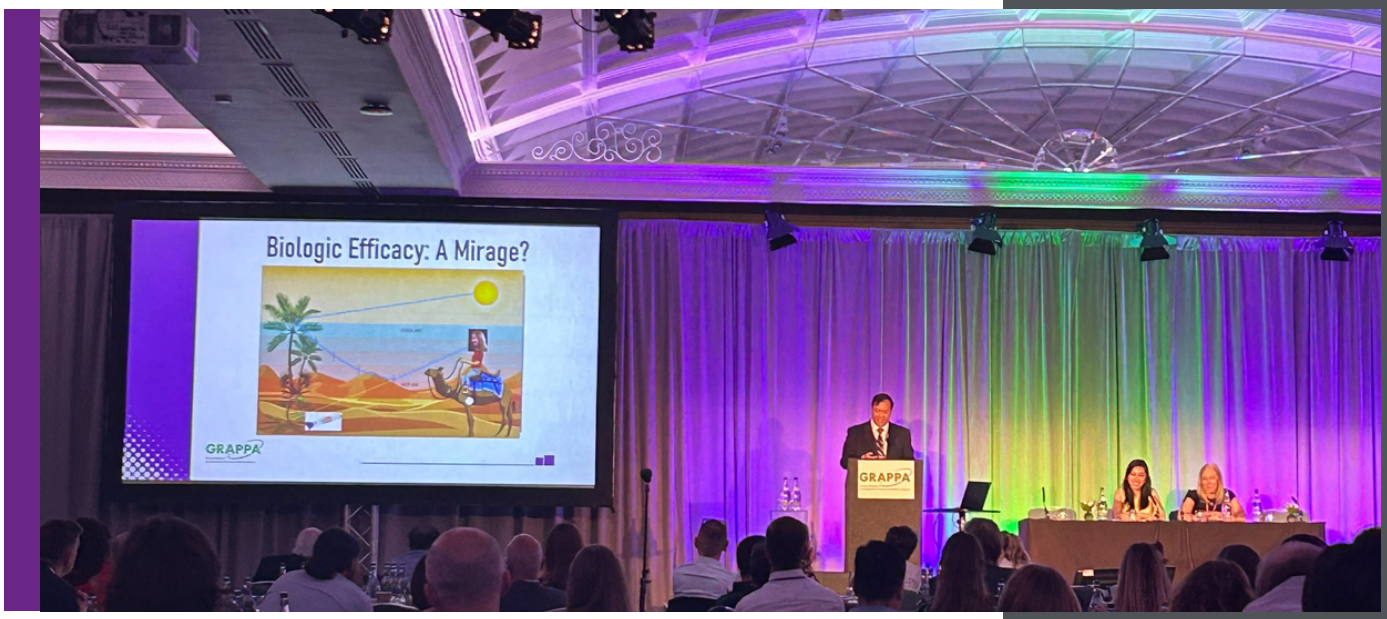
The enthesitis theory of PsA was proposed in 1998 based on imaging detected, but clinically non-demonstrable entheseal abnormalities in early PsA and SpA. **Dr. Dennis McGonagle, UK**, argued for the increasing evidence over the last 25 years supporting the enthesitis theory:

-Many studies have shown a high burden of imaging detected subclinical enthesopathy in psoriasis.
-Studies have also shown that such imaging abnormalities predate a diagnosis of clinical PsA.
-Many animal models with PsA features start at the enthesis before spreading to the synovium and bone e.g. TNF transgenic models and IL-23 minicircle model.
-The description of the synovio-entheseal complex in 2007 gave a unified concept for how entheseal inflammation manifests as synovitis.

In his counterargument, **Dr. Bruce Kirkham, UK,** highlighted the impact the enthesitis theory has had on the field in:

-Raising the awareness of the differences of PsA and peripheral SpA to RA, which was the main focus of research at the time.
-Generating a deeper understanding of the pathophysiology of PsA and peripheral SpA.
-The work on the synovio-entheseal complex suggesting that this might be the way that these arthropathies begin, in addition to being an important clinical component of these conditions.

Dr. Kirkham acknowledged that a growing field of animal models and human studies show that the enthesitis theory is probably true in some situations. In others, however, entheseal inflammation is not detected by sensitive imaging modalities such as US or MRI. Thus, the enthesitis theory has moved the field forward, but enthesitis does not drive synovitis in all cases of PsA.



DEBATE: TARGETED SMALL MOLECULES VS. BIOLOGICS AS FIRST-LINE SYSTEMIC THERAPY AFTER CONVENTIONAL THERAPY

In this debate, **Dr. Wilson Liao, US,** argued that oral small molecules (apremilast, deucravacitinib, and if PsA is present, upadacitinib or tofacitinib) should be first-line therapy after conventional therapy for moderate-severe psoriasis:

• Oral therapies are generally preferred by patients.
• Apremilast has a superior safety record with no substantial concern regarding infection.
• Deucravacitinib has comparable efficacy to TNFi like adalimumab.
• There is no association with immunogenicity or injection site reactions with oral therapies.
• Apremilast is approved for PsA; deucravacitinib has excellent emerging phase III data for PsA.
• Oral therapies may provide more worldwide and equitable access. Biologics are expensive, challenging to manufacture and store, and result in biohazard/waste.

Dr. Kristina Callis Duffin, US, presented the opposing argument, that biologics should be used after conventional therapy:

• All biologics except etanercept have clear superior efficacy by PASI 75 and PASI 90 at primary endpoints, with some demonstrating high rates of sustained PASI 90 through 5-year extension studies.
• Despite needing to be administered by injection, the infrequency of dosing appeals to patients with minimal coaxing or training.
• Safety data for 5-20 years do not show cumulative risks. IL12/23i and IL23i have excellent safety profiles without risk of some of the rare concerns with biologics (MS with TNFi, IBD with IL17i).
• Good evidence for efficacy in different PsA domains, and different psoriasis phenotypes.
• Many biologics are approved for children (not true of any small molecules).
• TNFi protect against cardiovascular disease, while JAKi (and possibly TYK2i) are relatively contraindicated in patients with cardiovascular disease. Venous thrombo-embolic risk is known with JAKi and more data are needed for TYK2i.

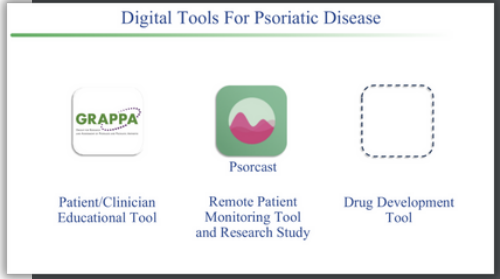
DIGITAL TOOLS FOR PSORIATIC DISEASE

Dr. Dan Webster, US, presented on Digital Tools for Psoriatic Disease:

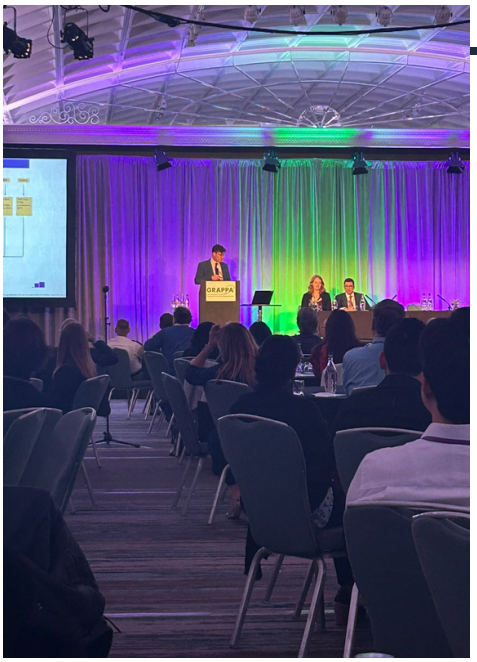
• There is a tremendous opportunity for an organization like GRAPPA to create and validate digital measurement tools that can be used by patients or physicians.

• Digital measurement tools, particularly those implemented on smartphone devices, can provide remote and frequent assessments of skin, nail, and musculoskeletal manifestations of psoriatic disease.

• There are currently no approved digital drug development tools for psoriatic disease.



DEBATE: SHOULD METHOTREXATE BE THE FIRST SYSTEMIC IN PSORIATIC DISEASE?



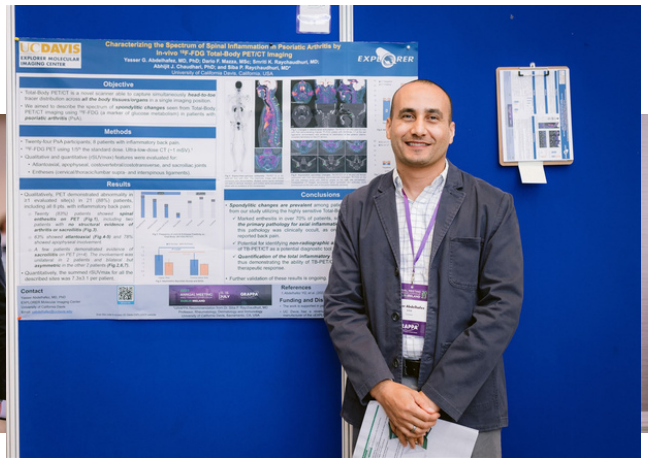
MTX is the most prescribed first-line systemic therapy for psoriatic disease and **Dr. William Tillett, UK,** argued that this practice should continue:

-Despite MTX achieving lower efficacy rates compared to biologics, 22.5-36% of patients achieve MDA.
-While MTX failed to produce significant differences compared to placebo in the MIPA trial, MTX may have been underdosed in this study.
-About 60% of patients in the Complete-PsA trial achieved MDA when taking MTX in addition to leflunomide, suggesting improved efficacy when combined with other therapies.
-Regarding safety and tolerability, up to 90% of patients do not experience nausea, and other adverse event rates are similar to those of biologics
-MTX is cheap - 15 pence per 2.5mg tablet.

Thus, the efficacy of MTX in some patients at a low cost justifies the use of MTX as the first-line systemic treatment for psoriatic disease. However, clinicians can and should quickly move on to other treatments for patients who experience low efficacy and/or side effects.

Dr. Joseph F. Merola, US, represented the opposing side and presented evidence that MTX has inferior efficacy and tolerability compared to newer systemic therapies:

-MTX failed to improve tender/swollen joint counts in the MIPA trial, and there is no convincing evidence that MTX inhibits radiographic progression of PsA.
-Dose escalation of MTX only has marginal benefit in patients who have failed MTX 15mg.
-The number needed to treat to achieve PASI 90 is 43.5 for MTX compared to 1.4-4.8 for newer target therapies.
-MTX and TNFi combination therapy is of modest if any benefit over TNFi therapy alone, and there is no benefit combining MTX with IL-17i or other newer targeted therapies.
-1/3 of patients stop taking MTX due to intolerance, often due to gastrointestinal symptoms or abnormal laboratory values.
-Patients taking MTX are three times more likely to experience nausea compared to placebo.
-27% of patients with psoriasis develop liver enzyme abnormalities on MTX.
-The frequent blood monitoring required with MTX is an inconvenience for patients.



UPDATE ON GRAPPA ULTRASOUND PROJECTS AND FUTURE DIRECTIONS

1. The DUET study
   - The progress of DUET, which aims to develop a diagnostic sonographic score for enthesitis in PsA that discriminates it from non-PsA, was presented by **Dr. Lihi Eder, Canada** (see page 8).

2. A systematic literature review on the prevalence and definitions of sonographic elementary lesions for articular and extra-articular structures in psoriatic disease.
   - Six groups comprising two Y-GRAPPA members under the supervision of a group leader will review the literature to evaluate the prevalence and definitions of synovitis, erosions, flexor mechanism lesions, extensor mechanism lesions, small entheses lesions and subcutaneous tissue lesions in psoriatic disease.

3. A survey on the availability of musculoskeletal ultrasound (MSUS) for psoriatic disease among GRAPPA members and the unmet needs.
   - This study aimed to understand how often MSUS is used in psoriatic disease among GRAPPA members, identify the barriers to MSUS use, and any inequalities to MSUS access.
   - 102 participants responded to the survey, and the results were recently published in Clinical Therapeutics.

4. Handheld US devices in Rheumatology – Are we there yet?
   - The aim is to compare the performance of a conventional stationary US device versus a handheld US device for scanning joints, entheses, tendons and nails in PsA.
   - Moderate agreement was achieved on an interim analysis based on the reading of images for the first 10 patients, allowing the study to proceed to the next phase.

BASIC SCIENCE WORKSHOP: ANIMAL MODELS - WHAT TO EXPECT FOR PSA & PSO

Animal models provide great opportunities to understand the disease pathogenesis and its cellular/molecular mechanisms. **Dr. Margot van Mechelen, Belgium, and Dr. Siba P. Raychaudhuri, US,** discussed how animal models of psoriatic disease can explore: (i) The inflammatory proliferative cascades of psoriatic disease and (ii) Develop novel, effective and safe therapies for psoriasis and PsA.

There is no known naturally occurring psoriatic disease in non-primates. Currently used animal models – almost exclusively rodent models – mimic certain aspects of the disease but are never a perfect representation. The number of animal models displaying both skin and joint inflammation is limited. Advantages and limitations of each model should be considered when planning studies.

Animal models for psoriasis can be developed by tissue-specific overexpression of targeted genes or loss of function approaches by using the knockout models. Also, the imiquimod topical application and the SCID mouse human skin xenograft models are widely used for drug development of psoriasis.

Models of PsA include (i) the minicircle-driven IL-23 overexpression mouse model which develops cutaneous lesions, axial and peripheral arthritis (ii) the spontaneous ankylosing enthesitis model in DBA/1 mice, and (iii) the beta-glucan driven arthritis and spondylitis in SKG mice.

Environmental factors like mechanical loading and diet can be studied under controlled circumstances in animal models. Results of these experiments can be used to optimize the design of randomized controlled trials in humans.

Ongoing technological advances offer more in-depth analysis, and especially high-resolution imaging techniques like microPET/CT become more widely available.

After this general discussion of animal models, Dr. Raychaudhuri shared his seminal work on the use of the animal models of psoriasis and PsA for development of T cell targeted therapies for autoimmune diseases.

PPP/CNO/SAPHO UPDATE WORKSHOP

Drs. Philip Helliwell (UK), Kristina Callis Duffin (US), and Bing Thio (The Netherlands) provided their perspectives and updates in SAPHO (Synovitis, Acne, Pustulosis, Hyperostosis, Osteomyelitis), CNO (Chronic non-bacterial osteomyelitis), PPP (palmoplantar psoriasis), and the role of the neutrophil in these disorders.

SAPHO and CNO are rare autoinflammatory/autoimmune conditions seen in adult and childhood patients. Histologically they are characterized by extensive neutrophilic infiltration. These conditions exhibit both innate and adaptive immune responses and share similar pathogenic molecules, and hence treatment targets. Treatment for SAPHO/CNO is largely empirical as this is an 'orphan' disease. Similarly, PPP and other neutrophilic skin diseases are uncommon, overlapping, and challenging to diagnose and treat. New developments in this field include the following:

- The OMERACT Working Group has made progress toward a core set of outcomes for clinical trials in SAPHO/CNO (including a scoping review, focus groups of patients, on-line discussion boards and a Delphi exercise yielding a reduced list of candidate core domains.
- Anne Leerling and Elizabeth Winter have made progress in achieving consensus on diagnosis and treatment. Several Delphi rounds are complete, with an upcoming in-person meeting for October 2023.
- ACR and EULAR have developed new classification criteria for childhood CNO.
- The C3 organization (CHORD-COUSIN Collaboration) has working groups aimed at core outcome sets and classification for PPP and related neutrophilic dermatoses.

The neutrophil is a phagocytic inflammatory leukocyte, central to the dysregulated inflammatory response in SAPHO, CNO, and neutrophilic dermatoses.

- Neutrophils play a key role in innate immunity and host response, and when tissues are infected, they are recruited from circulation to phagocytize pathogens. Their receptors recognize microbial structures to facilitate phagocytosis.
- SAPHO and related diseases have in common an autoinflammatory response, where pro-inflammatory cytokines (IL-1β, IL-17,TNF-α) are overexpressed and promote neutrophil recruitment into tissues. Homing to specific tissues is dependent on interaction with endothelium cells, adhesion molecules extravasation and migration into specific tissues.
- Modulation of neutrophil recruitment and function is crucial for future targeted therapies of SAPHO syndrome.

BIOMARKERS IN PSA AND PSO: WHERE ARE WE NOW?

Biomarkers for defined clinical outcomes have the potential to improve clinical outcomes and address unmet needs in patients with a heterogeneous condition like psoriatic disease. **Dr. Vinod Chandran, Canada,** gave an update on biomarker research in psoriatic disease. To date, molecular markers associated with clinical outcomes include:

- Predictive markers for PsA: CXCL-10, HLA-B alleles
- Diagnostic markers for PsA: CRP, MMP-3, OPG
- Treatment response: CRP, HLA-C*06
- Disease activity: CRP
- Joint damage: CRP, MMP-3
- Cardiovascular disease: Cardiac troponin I and NT-proBNP

Dr. Chandran highlighted challenges of biomarker research, including the definition of clinical endpoints, phenotypic heterogeneity, lack of phenotype data, differences in biospecimen collection and harmonization, data integration, analysis and management, and financial resources.

To overcome some of these, and move the field from discovery to verification, concerted international efforts are underway. These include HIPPOCRATES (see project update page 8), AMP and IPART.

OBESITY – A PANDEMIC IN SLOW MOTION

Dr. Donal O'Shea, Ireland, focused his talk on how our understanding of obesity has moved on and how much better we now understand how the body regulates weight. We now know that for 90% of people weight gain is 90% irreversible. Adipose tissue thermogenesis regulates this process and is influenced by medication – contributing to medication induced weight gain.

Understanding this interaction between medication and weight helps with empathy in raising the issue of weight and allows a positive start to address weight reduction with realistic goal setting and less self-stigmatisation.

INFLAMMATORY BOWEL DISEASE IN PSORIASIS

Inflammatory bowel disease (IBD) is more common in people with psoriasis than in the general population, with a prevalence of 1-2% and 0.4% respectively. Gastroenterologist **Dr. Edel McDermott, Ireland,** gave practical clinical advice:

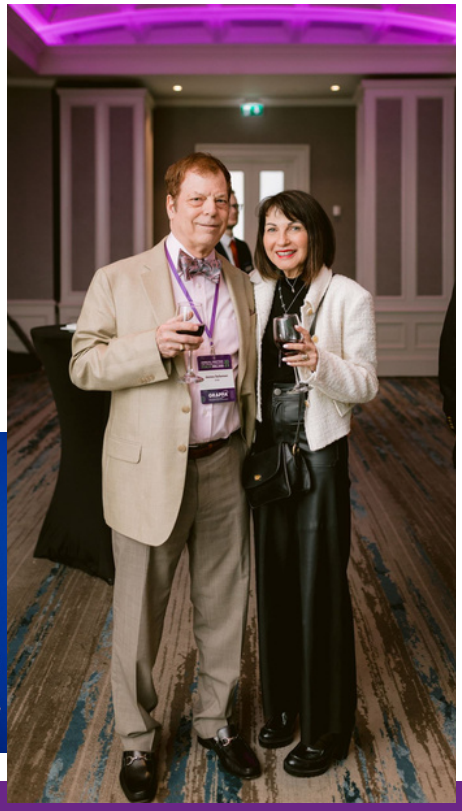
- Irritable bowel syndrome is more common than IBD and is common in young females. Symptoms include abdominal discomfort and change in bowel habit/form.
- Beware of new onset GI symptoms in individuals >40 years, nocturnal symptoms, and rectal bleeding. Refer these patients to gastroenterology.
- Faecal calprotectin can be useful – it is very sensitive for colonic inflammation but is not specific, and medications such as proton pump inhibitors and NSAIDs can give an indeterminate level (50-200 mcg/g).
- Caution with IL-17i and Etanercept in patients with IBD risk factors.

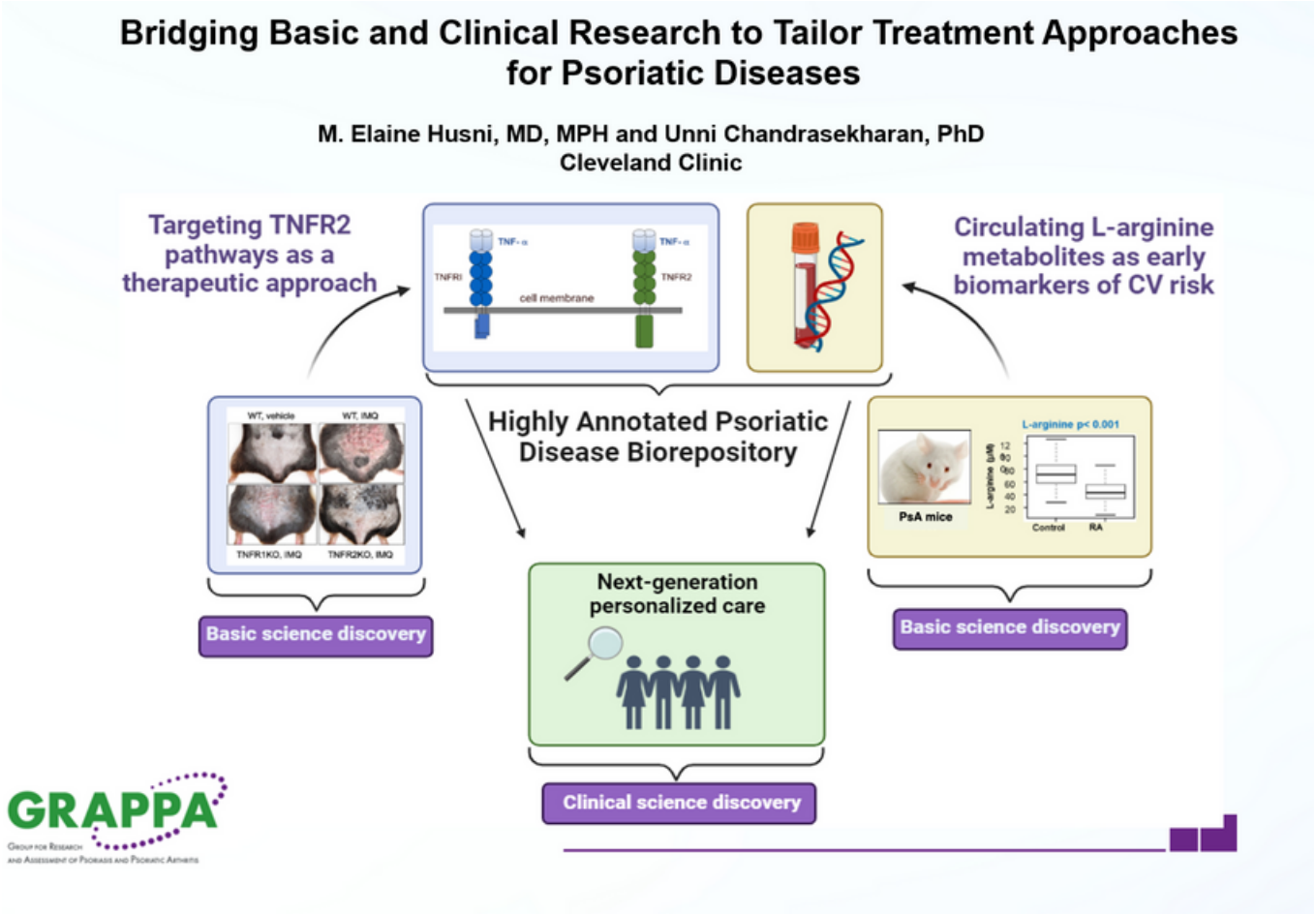
SPINAL LESIONS IN AXIAL PSORIATIC DISEASE: HOW SHOULD THEY BE IDENTIFIED AND QUANTIFIED BY MRI?

Dr. Mikkel Østergaard, Denmark, and Dr. Walter Maksymowych, Canada

Take home messages:

1. MRI is the method of choice for evaluating axial involvement in PsA.
2. No consensus definition of axial involvement in PsA yet exists.
3. ASAS have recently published MRI-definitions of inflammatory and structural lesions in the spine.
4. When assessing PsA patients for axial involvement, it is important to assess both vertebral body lesions and posterolateral lesions (such as inflammation in facet joints and costovertebral joints, and enthesitis at spinous and transverse processes).
5. The Canada-Denmark system is the preferred method for detailed evaluation of inflammation and structural damage at various anatomical locations in the spine, and it is reproducible and sensitive to change.





TARGETING THE CHEMOKINE RECEPTOR CCR6 IN PSORIASIS AND PSA

A family of proteins called chemokines and their receptors, particularly CCR6, play a role in psoriasis. **Dr. Sam Hwang, US**, presented how knowledge of CCR6 biology has been used to expand our therapeutic options for psoriatic disease, including a novel engineered chemokine that blocks CCR6-directed migration:

–CCR6 is expressed by Th17 and γδ T cells in human psoriasis and in mouse models of psoriasis where it is required for trafficking of pathogenic T cells.

–Disruption of CCR6 or blockade of function with antibodies to its ligand CCL20 or with engineered proteins prevent full induction of psoriasiform dermatitis (histologically and molecularly).

–Engineering of CCL20 into a dimeric molecule called CCL20 locked dimer results in antagonism of CCR6 function in vitro and in vivo with therapeutic implications for psoriasis and PsA.

UNINTENDED CONSEQUENCES OF THERAPY

PARADOXICAL PSORIASIS

Presented by **Dr. Elizabeth Wallace, US**

Paradoxical psoriasis is the appearance of a psoriasis subtype that occurs as a side effect of TNFi treatment. This has been described with all TNFis but is most common with infliximab and is seen during treatment for various autoimmune conditions, including rheumatoid arthritis, inflammatory bowel disease, and hidradenitis suppurativa.

Clinicians should be on the lookout for new onset psoriasis when treating with TNFi, though a flare of preexisting psoriasis can develop as well. The most common subtypes are pustular psoriasis, plaque psoriasis, and palmoplantar pustular psoriasis. Psoriasiform dermatitis, an overlap between eczema and psoriasis clinically and histologically, is another presentation of this phenomenon.

The pathophysiology of paradoxical psoriasis has not been fully elucidated, though an abnormal type I interferon response has been proposed to contribute to its development. Treatment algorithms have been proposed and clinicians should consider both the severity of the new onset psoriasis as well as the degree of control of the underlying disease for which the TNFi is being used when developing a therapeutic plan.

ENTHESITIS SEEN IN DUPILUMAB-TREATED PATIENTS

Dupilumab is a human IgG4 monoclonal antibody that blocks the functions of IL-4 and IL-13, key pathological pathways in atopic dermatitis. **Dr. Bruce Kirkham, UK**, presented their experience of 470 patients starting dupilumab: 36 were referred to rheumatology, with 26 (14 male subjects, 9 female subjects) exhibiting symptoms or signs of an inflammatory enthesitis, tenosynovitis, arthritis musculoskeletal syndrome similar to PsA.

Enthesitis findings were confirmed by ultrasound and MRI, with MRI reported sacroiliitis in one patient. Most patients had mild symptoms responding to NSAIDs or dupilumab dose reduction, but 40% had more severe symptoms that in many required stopping therapy. Most recovered but 10% had persistent symptoms 24 months after stopping dupilumab therapy.

They hypothesize that reduction of IL-4/IL-13 suppression of homeostatic inflammatory responses may have triggered musculoskeletal symptoms in susceptible individuals, which may also have been mediated by trafficking of pro-inflammatory cells from skin to musculoskeletal sites.

GRAPPA RESEARCH COMMITTEE

COLLABORATIVE RESEARCH NETWORK (CRN) ACTIVITIES

Following the recent restructuring of the GRAPPA leadership and committees, the activities of the research committee and the collaborative research network were merged into one research committee led by three co-chairs, **Dr. Vinod Chandran (Canada), Dr. Kurt de Vlam (Belgium) and Dr. Wilson Liao (US).** In addition to the co-chairs, the restructured research committee has 2 PRP, 1 Y-GRAPPA and 10 other members each serving for a 3-year term with one renewal.

Our mission is to facilitate global collaborative psoriatic disease research by fostering collaboration and co-operation between stakeholders worldwide. We will foster research projects initiated by GRAPPA members in collaboration either with other GRAPPA members or with our industry partners. We have developed a process by which research projects proposed by our members are formally endorsed by GRAPPA.

With the support from members of the research committee, we intend to provide support for the development of the research protocol, provide mentorship and ensure that the project is equitable, of high quality and has PRP involvement. The committee will also provide support for communicating and disseminating results to facilitate knowledge transfer and exchange. We will also continue to review and select up to four research grants for early career members that we hope will provide seed funds to set the stage for their research career in psoriatic disease.

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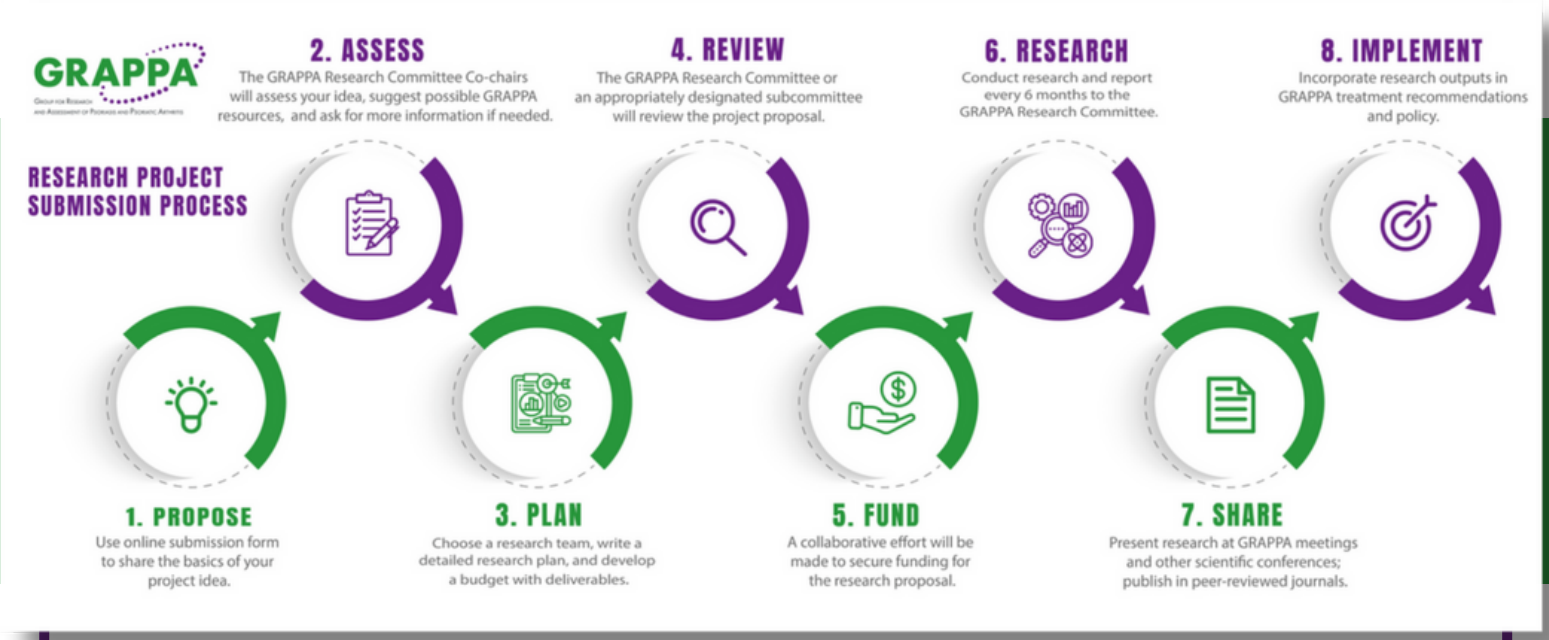
NEW PROCESS FOR RESEARCH PROJECT REQUESTS



YOUNG GRAPPA

Goals: boost networking within the Y-GRAPPA community and enhance collaborations with senior GRAPPA members/established GRAPPA projects.

The Future is Now: Y-GRAPPA members are involved in several GRAPPA projects and have created many Y-GRAPPA projects.

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MEMBERS SINCE 2021

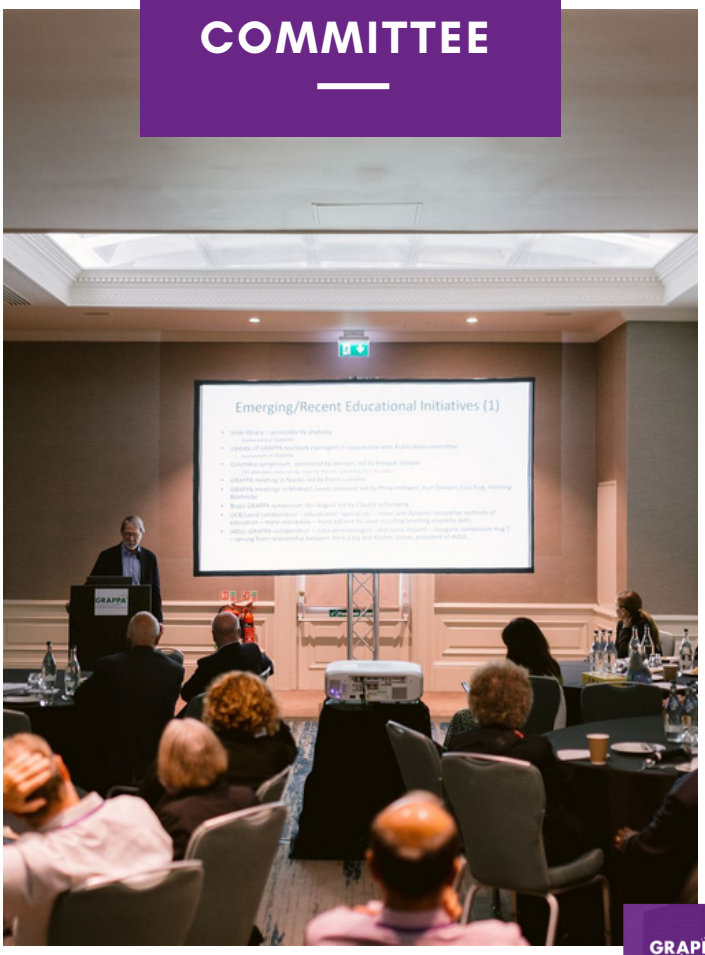
Your Turn: Encourage dynamic and passionate peers to join.

Let's broaden our community together!

How to become a member?

LEARN MORE HERE

EDUCATION COMMITTEE



RECENT AND EMERGING GRAPPA EDUCATIONAL INITIATIVES

- Slide Library – accessible to anybody.
- Update of GRAPPA textbook (Springer) in conjunction with Publication committee.
- Colombia Symposium, sponsored by Janssen, led by Enrique Soriano.
- GRAPPA meeting in Naples led by Ennio Lubrano.
- GRAPPA meetings in Mideast and Leeds (Janssen) led by Philip Helliwell, Kurt De Vlam, Luis Puig, Henning Boehncke.
- UCB/Lucid collaboration – educational "specialists" – novel and dynamic innovative methods of education – more interactive and patient-focused, including teaching empathy skills.
- IADVL-GRAPPA collaboration – sprung from relationship between Amit Garg and Rashmi Sarkar, president of IADVL.

- AFLAR meeting – GRAPPA representation/lecture by Ade Adebajo
- APLAR – GRAPPA symposium in Hong Kong led by Lai Shan Tam, Katy Leung, Peter Nash, Mitch Kishimoto, supported by Yoshia Tanaka
- APLAR memorandum of understanding to codify that each annual meeting will have a pre-meeting GRAPPA workshop and within meeting symposium
- PANLAR has had consistent GRAPPA symposia – discussion about memorandum of understanding
- Podcast "Inside GRAPPA" led by Fabian Proft and Gizem Ayan
- CME initiatives with Medscape and Paradigm
- Checklist to determine what educational symposia may be granted GRAPPA imprimatur

IDEOM Workgroup Meeting

The International Dermatology Outcome Measures (IDEOM) is a non-profit organization dedicated to advancing outcome measurements in dermatology. In a meeting adjacent to the 2023 GRAPPA Annual Meeting, IDEOM's Psoriatic Disease workgroup presented an update on their ongoing efforts.

Dr. Alice Gottlieb, US, presented preliminary results of an on-going research study aimed at evaluating the effectiveness of the IDEOM Musculoskeletal (MSK) symptom framework in a real-world clinical setting. In this study, all patients receiving dermatological care within the Mount Sinai Health System are now routinely completing the Psoriasis Epidemiology Screening Tool (PEST) and the Psoriatic Arthritis Impact of Disease (PsAID) questionnaires.

Dr. Joseph Merola, US, and Dr. Lourdes Perez-Chada, US, presented an update on the development and validation of the IDEOM MSK-Q questionnaire, a patient-reported questionnaire developed to capture the intensity and impact of musculoskeletal symptoms on quality of life in patients who have psoriasis with or without PsA (see page 11).

Dr. Vibeke Strand, US, summarized the proceedings of the Outcome Measures in Rheumatology (OMERACT) 2023 Conference.

Dr. April Armstrong, US, presented preliminary results of a multicentric study aimed at validating the DermSat-7 among patients with psoriasis (see page 9). Additionally, she introduced the development of the Psoriasis and Psoriatic Arthritis Treatment Satisfaction Instrument, which aims to evaluate patients' satisfaction with a therapy used to treat both their psoriasis and PsA.

Updates regarding the status of each of the described projects will be provided during the 2024 IDEOM Annual Meeting.

LEADERSHIP

BOARD OF DIRECTORS

WE THANK THE FOLLOWING STEERING COMMITTEE MEMBERS FOR THEIR YEARS OF SERVICE:

- Christopher Ritchlin, US
- Stefan Siebert, UK

WE WELCOME THE FOLLOWING NEWLY ELECTED MEMBERS:

Steering Committee:

- Lihi Eder, Canada (re-elected)
- Luis Puig, Spain (re-elected)
- Peter Nash, Australia
- Dennis McGonagle, UK

Derm Member-at-Large

- Laura Savage, UK

JOIN US NEXT YEAR!

NEWSLETTER CREDITS

The contributions to this Newsletter have been collected by the following Y-GRAPPiAns: **Dr. Gizem Ayan (Turkey), Dr. Tugba Izci Duran (Turkey), Dr. Hanna Johnsson (UK), Dr. Leonieke van Mens (The Netherlands), Dr. Raphael Micheroli (Switzerland), Dr. Debashish Mishra (UAE), Dr. Fabian Proft (Germany), Dr. Flavia Sunzini (UK) and Dr. Cemre Turk (US).**

Thank you to the presenters who wrote their own summaries. In addition, we are grateful for the summaries written by:

Dr. Gizem Ayan, Turkey: DUET and SAGE updates; Education group

Dr. Kristina Callis Duffin, US: PPP/CNO/SAPHO Update; Biologic for mild psoriasis - point/counterpoint

Dr. Tugba Izci Duran, Turkey: The history of GRAPPA

Dr. Hanna Johnsson, UK: AXIS, AxSpA and Treatment updates; Maria Shutova's pilot project presentation

Dr. Raphael Micheroli, Switzerland: Breakout session; Ruchi Shah's trainee talk

Dr. Stephen Pennington, Ireland: HIPPOCRATES

Dr. Sonia Sundanum, Ireland: US group

Dr. Flavia Sunzini, UK: Jaehwan Kim's pilot project presentation

Dr. Danielle Yee, US: DermSat-7 treatment satisfaction

Arianna Zhang, US: Methotrexate as first-line debate

Dr. Hanna Johnsson, UK, coordinated the work and edited the texts; **Annie Spangler, US,** put everything together with photos and links, and **Dr. Kristina Callis Duffin, US,** provided senior GRAPPA oversight.