

GRAPPA

GROUP FOR RESEARCH
AND ASSESSMENT OF PSORIASIS AND PSORIATIC ARTHRITIS

Annual Meeting July 14-16, 2022 - Brooklyn, NY



420 Attendees from 31 countries

Congratulations to the Research Grant Awardees 2022

COLLABORATIVE GRANTS - \$35,000

Jaehwan Kim, VA Northern California Health Care System
Comparative single-cell genomic profiling of synovial fluid versus skin lesions in psoriatic arthritis
Mentor: Siba Raychaudhuri

Lourdes Perez Chada, Harvard
Longitudinal relationships between sleep and symptoms in patients with Psoriasis and Psoriatic Arthritis
Mentors: Joseph Merola and Elizabeth Klerman

STANDARD GRANTS: \$25,000

Tejpal Gill, OHSU, Portland
Characterizing the effect of HLA-B27 on gut microbial dysbiosis in axial psoriatic arthritis
Mentor: Atul Deodhar

Maria Shutova, University of Geneva
The role of mechanotransduction in hyperactivation of TGF- β via α V β 6 integrin in psoriatic epidermis
Mentor: Wolf-Henning Boehncke

David Simon, University Hospital Erlangen, Germany
Assessing the impact of different treatment strategies on damage progression and functional decline in Psoriatic Arthritis
Mentor: Georg Schett



GRAPPA Executive Retreat 2022

Oliver Fitzgerald

On the day before the annual meeting began, 36 enthusiastic GRAPPA Executive/Steering committee members and a small number of invited others gathered for the day, facilitated by Ruth Nicholson. Dafna Gladman gave an entertaining and informative review of the organization which celebrates 20 years in existence next year. April Armstrong reviewed the 2016 retreat output and the results of a pre-2022 meeting survey of attendees on the achievements of GRAPPA since 2016. While achievements in education and research scored highly, it was clear that the organizational structure hadn't sufficiently kept up with these achievements. A discussion then took place on organizational objectives for the next five years together with a step-by-step identification of what will be required to achieve the objectives. Oliver FitzGerald presented a proposal for organizational change with four pillars of the GRAPPA organization: Finance, Education, Research, and Governance. Modifications to the proposed structure were made during the lively discussion. The proposed changes likely will necessitate changes to the GRAPPA bylaws and will take some time (3-6 months) to implement. The proceedings of the 2022 GRAPPA retreat will be published, and GRAPPA members will be kept informed of the changes being proposed.

This year, 43 abstracts were submitted from 14 countries. After review, five were selected for oral presentations and 15 for poster presentations. Read on to learn more.

Young GRAPPA



Hanna Johnsson and Fabian Proft

The GRAPPA Annual Meeting was a great success and a great pleasure for all Y-GRAPPIAns joining!

At the Y-GRAPPA and Trainee Networking Workshop Fabian Proft (Germany) welcomed everyone as the chair for Y-GRAPPA. After a short overview on the activities of the last months, he handed the podium over to the Y-GRAPPIAns Janne Bolt (The Netherlands), Silvia Scriffignano (Italy) and Dimitri Luz (Brazil), who presented cases. They generated interdisciplinary and lively discussions within the group. Both Rheumatology and Dermatology participants gained new insights from each other's perspectives and really enjoyed the face-to-face encounter! The case discussion was followed by short updates from our different subgroups:

Education: Gizem Ayan (Turkey) and her team were congratulated on the completion of short video interviews with GRAPPA members. The videos were launched on Twitter and played on large screens during the annual meeting. Current work of the group is focussing on updating the GRAPPA Slide Library.

Dermatology/Rheumatology collaboration: Dimitri Luz (Brazil) and Hannah Jethwa (UK) encouraged all to continue the campaign, "Bring a Derm friend," and we discussed new ideas for this important group.

Governance: The Governance group, led by David Simon (Germany), will work on the Y-GRAPPA mission statement and bylaws.

Networking: Attendees at the annual meeting very much enjoyed a first face-to-face networking event, which was organised by the group, led by Arani Vivekanantham (UK). Further events will take place adjacent to meetings such as the ACR. In addition, virtual mentor-mentee meetings are planned for the Autumn.

Newsletter: Our first Y-GRAPPA newsletter was circulated in April and the group, led by Hanna Johnsson (UK), will help to prepare the Newsletter reporting on the annual meeting.

Social media: Participants discussed the use of different social media platforms for different purposes and audiences and suggested that there should be an official GRAPPA LinkedIn account, along with the @Grappa0 twitter account. In addition, Y-GRAPPA brainstormed to open their own Instagram and Facebook accounts. In time, these could for example be used to post monthly case presentations to generate interdisciplinary derm/rheum discussions. The group will, under Sebastián Herrera's (Colombia) lead, formulate SOPs for how official Tweets should be written.

Research: The research group has two new team leaders: Michelle Mulder (The Netherlands) and Rachel Grynspan (Brazil). They will work to get Y-GRAPPIAns actively involved in GRAPPA research projects and aim to start Y-GRAPPA research projects in the future. Fabian Proft encouraged each group to focus on one priority project to be completed in 2022.

We look forward to seeing everyone as soon as possible to foster networking within our group and shape the started collaborative projects!



Pilot Research Grant Recipients

Therapeutic Exploration of Probiotic Strain *L. reuteri* in Western-diet-induced Psoriatic Skin Inflammation

Daisuke Yamada

Literature suggests that diet affects the severity and incidence of human psoriasis, but the underlying mechanisms remain unclear. In our previous study using an experimental mouse psoriasis model with IL-23 minicircle DNA (IL-23MC) we found that change in the gut microbiota due to Western diet (WD) amplified inflammation. As literature suggests certain probiotics may reduce inflammation, we hypothesized that probiotics may restore the dysbiosis observed in WD fed mice. Oral gavage of the probiotic *L. reuteri* improved IL-23MC-induced skin inflammation in mice. However, these mice showed more severe fatty liver compared to non-treated mice, suggesting that liver changes may limit the long-term utility of *L. reuteri*.

Facilitating Assessment and Treatment of Psoriasis in Rheumatology Clinical Practice

Fazira Kasiem

Psoriasis severity throughout the first year after diagnosis of PsA is mostly mild in patients seen in daily clinical practice but impacts health-related quality of life (HRQoL). Results of our studies have shown that approximately 50% of patients who reached musculoskeletal low disease activity one year after their diagnosis have not reached psoriasis remission. While their skin burden is generally low, around 30% still experienced considerable skin burden which can only be measured using a dermatology-specific rather than a general HRQoL questionnaire. To facilitate assessment and treatment of psoriasis in daily rheumatology clinical practice, we developed a practical guide to assessing both impacts of psychosocial and physical symptoms. Rheumatologists should continue assessing skin burden and treating psoriasis in PsA patients, irrespective of musculoskeletal disease activity.

Cross Sectional Study on Differences in MRI Appearances of Spinal Involvement in Patients with Axial Spondyloarthritis vs. Axial Psoriatic Arthritis

Josefina Marin

It is unclear whether magnetic resonance imaging (MRI) appearances of spinal involvement differ between patients with Axial Spondyloarthritis (SpA) and patients with Axial PsA. All patients underwent a clinical evaluation and MRI of the sacroiliac joint (SIJ) and spine. Patients treated with biologics were excluded. Our preliminary data indicate that PsA patients have more enthesitis (MASES ≥ 1 40% vs. 6% $p < 0.00$), higher mean body mass index (BMI), and higher BASDAI than SpA patients. SpA patients had a higher percentage of positive HLAB27 than PsA patients (67% vs. 22% $p < 0.01$).

There were no differences in:

- Inflammatory changes in spine (CANDEN)
- Structural changes in spine and SIJ (SSS and CANDEN)
- Asymmetry at the SIJ (X-ray and MRI)

There were differences in:

- Inflammatory changes in SIJ (81% SpA vs. 55% PsA $p \leq 0.03$)
- The prevalence of isolated inflammatory spine involvement (21% SpA vs 43% PsA $p = 0.015$)
- Positive correlation between CPR and SPARCC SIJ in SpA



Basic Science



Getting to Individualized Diagnosis and Treatment for Psoriasis and Psoriatic Arthritis

Stephen Pennington

To date the track record of biomarker development to clinical utility has not been overly impressive. This is in part due to use of poor clinical specimens for biomarker discovery, a fragmented approach to the biomarker roadmap – from discovery through development to utility (delivery), and too much emphasis on biomarker ‘omics technologies rather than unmet clinical needs.

Perhaps the key to biomarker success begins with identification and detailed assessment by scientists, clinicians, and individuals with PsA of an unmet clinical need for which the biomarkers will be used. An often overlooked step is the ‘validation’ of the unmet need with the views/opinions of an independent group from those who identified it. Once ‘validated’ the unmet need and proposed intended use should guide the discovery and evaluation of candidate biomarkers. The key unmet needs in PsA include biomarkers that can predict individual response to treatment.

Existing biomarkers often consist of one type of molecule (DNA, RNA, protein, metabolite etc.). Multiple omics technologies are now being used to identify molecular biomarkers. Biomarker ‘signatures’ and associated algorithms provide the individual and their healthcare physicians with reliable and easy to interpret ‘scores’. Multi-omics strategies are now being applied across a range of auto-immune diseases, including PsA with the recent launch of the project ‘HIPPOCRATES’. HIPPOCRATES is a European private-public consortium of 26 partners funded by the EU’s Innovative Medicines Initiative. Through access to clinical samples with associated detailed clinical phenotypic data at an unprecedented scale, HIPPOCRATES predominantly seeks to identify, evaluate, and validate multi-omic biomarkers to develop diagnostic algorithms. These algorithms should address the key unmet needs in psoriatic disease and be made ready for clinical implementation. The HIPPOCRATES project is highly complementary to the very recent FNIH AMP AIM project which seeks to use omics technologies, including single cell approaches, to inform a better understanding of psoriatic disease mechanisms.

One exciting future opportunity lies in development and implementation of large-scale longitudinal studies which may support the identification of ‘personalised biomarkers’ to predict treatment response in individuals. Early identification of PsA in individuals with psoriasis provides opportunity to intervene early with the most effective treatments. Achieving biomarker success will likely require continued engagement with all stakeholders, international collaborations, incentivization of participants, including appropriate rewards for high-quality data, and contributions that align with the overall objective of improving the outcomes of those with PsA. Project management, financial management, marketing, and liaisons with regulatory and legal agencies are also required. We collectively have a huge opportunity to have impact on patient outcomes if we have the will to dismantle the many obstacles and do it.

Basic Science

Total Body PET/CT to Measure Degree of Inflammation in Psoriatic Arthritis Patients

Siba Raychaudhuri

Total Body (TB)-PET/CT captures radiotracer uptake across the entire body. Radiotracer uptake data provides standardized measures for the degree of inflammation. Our overall hypothesis has been that TB-PET/CT measures will (1) offer unique insight into systemic PsA inflammatory domains and (2) provide biomarkers (SUVmax) that will quantify the degree of inflammation and thus associate with PsA disease activity, such as with DAPSA (Disease Activity index for Psoriatic Arthritis).

With the help of a pilot grant from the National Psoriasis Foundation we explored the merits of a TB-PET/CT scan to develop a diagnostic test for PsA. The objective of our study was to identify and quantify the degree of inflammation and structural damage from TB-PET/CT imaging and correlate it with the five clinical domains of PsA (arthritis, enthesitis, dactylitis, and spinal and nail inflammation).

We have prospectively recruited and completed scanning of participants with PsA (n=20), rheumatoid arthritis (RA) (n=20), and osteoarthritis (OA) (n=20). Our results indicate that TB-PET/CT measures can identify unique pathologies of PsA that differentiate PsA from RA and OA. Our preliminary findings demonstrate that with TB-PET/CT imaging we can identify and quantify the degree of musculoskeletal inflammation of five clinical domains of PsA including synovitis, enthesitis, dactylitis, and inflammation of spine and nail matrix.

Compared to blood or genetic markers as diagnostic tools, TB-PET/CT imaging provides an addition to diagnose certain critical quantitative parameters such as severity and extent of the disease in each patient. Additionally, TB-PET/CT identifies subclinical underlying pathology, which makes it an ideal testing tool for early diagnosis at the transition point from psoriasis to PsA.



Basic Science

Single Cell Omics of Psoriatic Disease: An Update

Joy Q. Jin and Wilson Liao

In the last few years, single-cell experimental techniques have gained widespread popularity and enabled researchers to study the features of individual cell-cell interactions in numerous autoimmune conditions. These techniques have yielded particularly intriguing results when studying in detail the immunomodulatory mechanisms leading to psoriasis and PsA development.

The single cell studies discussed in Dr. Liao's presentation can be summarized into five key takeaways. Firstly, a small subset of cells, such as IL-17+ CD4+ or CD8+ T cells can have an outsized impact on the development of psoriasis. These cells may represent less than 10% of T cells in psoriatic skin yet showed enriched expression of multiple effector functions.

Second, multiple cell types appear to play a supporting role in psoriasis pathogenesis, highlighting the heterogeneity of immune dysregulation involved and providing more complex revisions to the original psoriasis disease paradigm. Important cell types include CD14+ dendritic cells and CCR1+ macrophages that produce IL-23A, keratinocytes that produce IL-36, Mac2 macrophages, and VE3 vascular endothelium cells that produce chemoattractants and adhesion molecules.

Third, cell states in psoriasis are fluid meaning they may have de-differentiating potential. Certain cell types may initially appear quiescent or atopic-dermatitis-like (type 2 cytokine profile) but can be triggered into a more psoriatic type 17 phenotype with environmental triggers.

Fourth, clonal T cells may be responsible for driving disease. Recent single-cell sequencing studies have most clearly demonstrated clonal expansions in PsA, where increased proportions of memory CD4+ and memory CD8+ T cell subtypes were found in synovial fluid samples.

Finally, machine learning models may benefit from single cell data. Such models enable us to take a step forward in identifying biomarkers for earlier identification of PsA or predicting response to biologic therapy.

Ultimately, single-cell techniques provide unparalleled insight into cell heterogeneity and the biological mechanisms driving psoriasis, PsA, and treatment resistance in both. We look forward to continued progress in the upcoming decade to enable improved diagnosis and treatment for psoriatic disease patients.

Biomarkers in the Clinic in 2030

Stefan Siebert

Biomarkers have the potential to transform clinical care and outcomes for people with psoriatic diseases. Large, exciting initiatives are underway in the EU (HIPPOCRATES and BIOMAP IMI Consortia) and the US (AMP ELLIPSS project) that will help identify biomarkers. Any biomarkers identified need to be validated and overcome regulatory hurdles, in addition to convincing payers of their value.

For the true benefit of biomarkers to be realized, they have to be integrated into clinical practice. In current clinical practice, we only see cross-sectional snapshots of patients' conditions when they attend clinic, with limited patient reported outcome (PRO) information to fill in the gaps. Simply introducing hospital-based biomarkers into this system will have undoubted benefits (e.g. selecting the optimal treatment), but will not lead to the true transformation required for these chronic, long-term conditions.

With advances in technology and the almost ubiquitous use of mobile phones, there are opportunities to remotely and routinely capture a range of clinically-relevant PROs and information from devices to give a far more complete picture of the current status and impact of these conditions. Technology includes wearables for continuous monitoring with "lab-on-skin", smart insoles, and at-home testing kits all examples with clear applicability for psoriatic disease.

These advances and technologies, including artificial intelligence, provide opportunities to generate an unprecedented amount of data about our patients and their conditions, but also present significant challenges. Data literacy has potential to exacerbate health inequalities, while data ownership and privacy remain real concerns. Traditionally, patient data has been held in hospital record systems, but in the future, patients may hold their healthcare data on their smartphones, so integrating this with hospital electronic health record systems and presenting data in an understandable and actionable format will be crucial.

The prediction is that by 2030 and beyond the future of biomarkers has to be patient-centric, that is organized around the patient and not the hospital or clinical team. This will require a major change in healthcare organization and culture. The importance of building trust and engagement with patients and involving clinicians and patient organizations in the move to this new way of working was highlighted in the discussion that followed this presentation.

Project Highlights



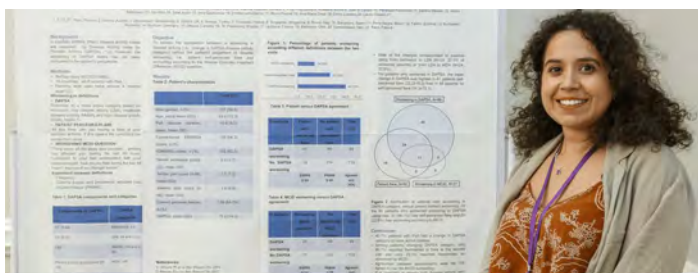
Report on Updated Treatment Recommendations

Laura Coates

The 2021 treatment recommendations were recently accepted for publication in Nature Reviews Rheumatology and are available open access. There are also eight manuscripts finalized and submitted to the Journal of Rheumatology that describe the literature review and detailed recommendations from each domain: peripheral arthritis, enthesitis, dactylitis, axial disease, skin, nails, related conditions, and comorbidities.

The next steps are to develop a patient-facing version of the treatment recommendations and to support dissemination of both sets of recommendations. The patient version of the recommendations is being led by Denis O'Sullivan with help from other GRAPPA Patient Research Partners. This will build on the version developed in 2015 with updates as necessary to cover new treatments and new information on comorbidities.

Dissemination work is already underway with the treatment recommendations. Talks and educational resources have been developed. The recommendations have been highlighted on the GRAPPA website and via GRAPPA social media accounts. So far, we have partnered with two external organizations to help this. RheumNow is an educational rheumatology website that has featured blogs about the recommendations and a live webinar. Guideline Central, with whom we partnered in 2015, have developed an updated quick reference guide of the treatment recommendations. The first printed copies of these were shared at the GRAPPA meeting and Guideline Central have partnered with several pharmaceutical companies to support distribution of these internationally.



Educational Initiatives

Jodi L. Johnson

Dr. Philip Mease presented a summary of the past, current, and future educational initiatives of GRAPPA. The Education committee is comprised of 19 members, including 4 PRPs, 2 Young GRAPPiAns, and a similar representation of rheumatologists and dermatologists with broad global representation. Their overarching initiatives include:

- educational symposia for rheumatologists and dermatologists around the world held both virtually and in person.
- development of a slide library: currently undergoing update by Y-GRAPPiAns in collaboration with mentors.
- creating physical examination educational videos that can be used by pharma or to train residents and fellows.
- development of podcasts in the future

Collaborations exist between GRAPPA and SPARTAN, ASAS, NPF, SAA, IFPA, pharma, and CME organizations, among others in development.

Recent activities have included a global education series with five virtual workshops in different time zones conducted in 2021 with a Pfizer grant. Rolling out in 2022, and also Pfizer funded, has been a collaboration to create three modules of clinician and patient-facing webinars and podcasts covering pediatric disease, pain and fatigue, treatment, and, just for patients, nutrition/diet/exercise/and wellbeing. Several symposia have been and are planned to educate rheumatologists and dermatologists on all aspects of psoriasis and PsA in various parts of the world, including India, Taiwan, Hong Kong, the Middle East, Europe and South and North America. These are generously funded by a number of GRAPPA's pharmaceutical sponsors. Symposia are also being held annually in conjunction with ACR, PANLAR, APLAR, and AFLAR. CME accreditation is applied where needed.

Emerging educational initiatives also include a new collaboration with UCB to create novel and dynamic innovative teaching methods with more interaction and patient-focused skills such as empathy and active listening. The GRAPPA textbook is being updated in conjunction with the Publication committee, Y-GRAPPiAns, and a medical writer.

A discussion followed the presentation about consent for images for the slide library. There will be follow-up on this topic prior to making images live in enduring material.

Improving Diagnosis and Outcomes for Psoriatic Arthritis

Looking for Psoriatic Arthritis in Psoriasis: A Dermatologist's Perspective

Cheryl Rosen

The prevalence of undiagnosed PsA is 10-15%. As PsA most often occurs after the onset of psoriasis, dermatologists are uniquely positioned to diagnose PsA early, thus preventing joint damage and worsening quality of life. To determine if the message that dermatologists can aid early diagnosis of PsA is being sent to dermatologists, a literature search was performed including review articles in dermatology journals in several languages and studies on screening tools, revealing 35 papers that highlighted this message. A particularly helpful review highlighted simple musculoskeletal (MSK) maneuvers a dermatologist can perform in clinic to determine the extent of PsA followed by a physician/patient discussion of the diagnosis and treatment.

While for many dermatologists, these practices are not realistic, the message that dermatologists can detect PsA is being heard. Dermatologists are either asking their patients several questions about MSK symptoms or using a screening tool. Dermatologists can ask the questions so that patients can be referred to a rheumatologist.

Dermatologists encounter several difficulties in adding screening for PsA to their evaluation of a person with psoriasis. These include: competing priorities during time limited consultations; unknown diagnosis at first visit so the patient is not screened in the waiting room; The need to prioritize dermatologic issues rather than wholistically approaching the patient; a sense of being overburdened; the need for annual screening, not just at the initial visit; lack of access to a rheumatologist referral. Questions remain about whether a dermatologist should order diagnostic tests for PsA such as XRays, MRI, or ultrasound. The appropriate expectation should be knowing when to refer, not to diagnose and treat PsA.



Ten Years After the CONTEST Study

Laura Coates

This presentation introduced screening questionnaires used to identify PsA amongst patients with psoriasis. We know that there is often a diagnostic delay in PsA and that people with psoriasis represent an “at risk” group. Delay in diagnosis has long term implications for those patients. Previous studies in outpatient dermatology clinics have identified people with undiagnosed PsA. Numerous questionnaires have been developed to try to facilitate screening for PsA in dermatology or primary care clinics. These have been compared in several head-to-head studies with no clear winner. They have relatively low specificity but clearly help to identify patients who have musculoskeletal symptoms and raise the awareness of PsA amongst people with psoriasis. They are relatively easy to implement with engaged dermatology teams, but given their low specificity, it may be worth combining the questionnaire with other information such as symptom impact, investigations, or further triage to ensure that referrals to rheumatology are not overwhelming.

Psoriatic Arthritis Screening Beyond Self-reported Symptoms

Lih Eder

With the limitations of questionnaires, the PRESTO study developed risk prediction models for PsA among patients with psoriasis to help improve early detection and facilitate early intervention.

The study analyzed data from the IPART cohort in Toronto that followed patients with psoriasis without arthritis at baseline from 2006 to 2019 and their PsA status was assessed annually by a rheumatologist.

The researchers created risk prediction models for 1-year and 5-year time periods. The models included a combination of patient reported outcomes (e.g. pain, fatigue), patient demographics (age, sex) and psoriasis characteristics (e.g. psoriasis severity, nail lesions). The accuracy of the models, as assessed by area under the curve (AUC), was reasonable with AUC of over 70% for both models and good model calibration. Work is underway to validate these models in external cohorts of psoriasis patients.

Overall, the study showed that the development of PsA within clinically meaningful time frames can be predicted with reasonable accuracy for psoriasis patients. These models offer opportunities for screening of high-risk psoriasis patients in clinic and research settings.

Improving Diagnosis and Outcomes for Psoriatic Arthritis

Debate on Early Use of Biologics to Prevent Psoriatic Arthritis

Alexis Ogdie-Beatty and Enrique R. Soriano

Moderator Arthur Kavanaugh, University of California, asked the audience if, “early aggressive treatment of psoriasis can prevent PsA”. The audience voted both “yes” and “no”.

Alexis Ogdie-Beatty, University of Pennsylvania, started the debate by stating, “We don’t know that biologics prevent PsA”. She argued that only observational studies currently support the rationale to use biologics to protect against the development of PsA. Observational studies are prone to biases including selection bias, confounding by indication, protopathic bias (related to temporal sequence), survival bias, and assessment bias. The decision to use biologics for patients with psoriasis is complex and depends on many factors, many of which are not recorded in administrative datasets or registries. Thus, patients prescribed different types of therapies cannot be directly compared, particularly to those who were not prescribed a therapy. From existing observational data, there is a higher incidence of PsA in psoriasis patients who recently started biologic treatment. This does not mean that biologics cause PsA. Rather, it may reflect that dermatologists are more likely to start systemic treatment if they think that patients are developing PsA and this may precede the coding of PsA by rheumatologists. The finding simply highlights one flaw of observational studies.

Dr. Soriano took the position that effective treatment of psoriasis with biologics can prevent the development of PsA. While it is true that evidence to support this position comes only from observational studies, Dr. Soriano applied Bradford-Hill criteria including consistency of findings from study to study, temporal sequence of the association, and biological plausibility upon which to build his argument.

Dr. Soriano pointed out that four retrospective cohort studies have explored this association. Three found a lower incidence of PsA in psoriasis patients treated with biologics compared with those treated with topicals or phototherapy. The fourth, a large study performed in the US by Meer et al., found that psoriasis patients treated with biologics have an increased incidence of PsA, which was the study mentioned by Dr. Ogdie-Beatty. Dr. Soriano argued that the biases in observational studies favor an increase in the incidence of PsA in patients receiving biologics. Although likely to be present in all the studies, biases could partially explain the Meer study findings of increased PsA. Dr. Soriano also argued for biological plausibility. First, subclinical, asymptomatic enthesitis, which can be effectively treated with biologics, is frequent in patients with psoriasis and a risk factor for developing PsA. Abolishing enthesitis through treatment with biologics might prevent development of PsA. Second, reduction of skin inflammation using biologics could reduce inflammatory cells in joints, thereby decreasing PsA.

Dr. Soriano concluded that current evidence supports treating psoriasis with biologics to decrease PsA. Dr. Ogdie-Beatty concluded that there is insufficient data to support this association. Both speakers agreed that more answers are needed using randomized controlled trials, some of which are underway.



Imaging Workshops

MRI Working Group – MRI of peripheral enthesitis

Mikkel Østergaard and Walter Maksymowych

Enthesitis is a key disease manifestation in PsA, which is poorly examined clinically. Its presence or absence is mainly determined based on degree of local tenderness. Objective visualization and evaluation methods to detect enthesitis are needed both for clinical trials and practice. MRI allows sensitive evaluation of both joints and entheses in PsA and other types of spondyloarthritis. MRI and ultrasonography both allow visualization of soft tissue, but MRI is the only imaging method that allows assessment of bone inflammation (osteitis).

An OMERACT scoring system has been developed and validated for use in clinical trials and observational cohorts (The HEMRIS method) for heel enthesitis (achilles enthesitis and fasciitis plantaris) through separately assessing intratendinous, peritendinous, and intraosseous components of enthesal inflammation. The scoring system has high reproducibility and sensitivity to change for its inflammatory components. However, detecting sensitivity to change of the structural damage components (bone erosion and new bone formation) requires cohorts with longer follow-up than currently available.

Entheses and joints of the entire body can be visualized by whole-body MRI. A scoring method has been developed and validated for whole body MRI (OMERACT MRI Whole-Body Score for Inflammation in Peripheral Joints and Entheses, MRI-WIPE). This system assesses synovitis and osteitis in 83 peripheral joints as well as soft tissue inflammation and osteitis at 33 entheses (0-3 grading per joint or enthesis). MRI-WIPE has good reliability and sensitivity to change. Discriminatory ability between spondyloarthritis patients treated with TNFi and placebo has been demonstrated.

The MRI workshop at GRAPPA 2022 described the MRI appearances and scoring methods of enthesitis. Through examples from patient cases, the workshop demonstrated the utility of MRI for improved assessment of enthesitis. The next step of the MRI working group is to apply the MRI techniques in larger clinical trials and cohorts of patients with PsA, to further develop and validate the MRI assessment systems.

Ultrasound (US) Steering Committee DUET Update

Lihi Eder, Gurjit S Kaeley, and Sibel Aydin

The Diagnostic Ultrasound Enthesitis Tool (DUET) project is a GRAPPA-supported study that involves 18 sites across the world. The study aims to develop a new sonographic enthesitis scoring system to help with early diagnosis of PsA. The study achieved its first major milestone of recruiting over 50% of its target (219 out of the planned 400 patients). The efforts of investigators to recruit and scan patients are very much appreciated. Interim analysis of inter-rater agreement found moderate to substantial agreement for most sonographic elementary lesions among central readers. Inter-rater agreement was not influenced by most patients' characteristics apart from obesity which may increase variability in scoring. It is anticipated that the recruitment of study patients will be completed by July 2023. Obtaining images with high fidelity is key to recognizing subtle features of enthesitis and improving reading reliability. Common pitfalls found in submitted images were reviewed.

Projects for the upcoming year include two ongoing systematic literature reviews identifying which joints need to be scanned in psoriatic disease using US and the value of scanning extra-articular structures in the diagnosis of PsA. The group is also working to validate a hand-held US device, with the hopes of increasing the accessibility of PsA patients to US, enabling earlier and accurate diagnosis. In addition, in 2023 there will be a position paper on the current role of US in psoriatic disease and the unmet needs among the GRAPPA members.



Axial Psoriatic Arthritis

Debate About the Identity of Axial Psoriatic Arthritis

Anand Kumthekar

On the final day of the GRAPPA meeting, Dr. Coates and Dr. Deodhar participated in an exciting debate with the premise, “Be it resolved that Axial Psoriatic Arthritis (axPsA) is Axial Spondyloarthritis with Psoriasis (axSpA)”.

Dr. Coates opened by highlighting important similarities between axPsA and the broader term axSpA, but acknowledged differences like HLAB27 positivity, peripheral disease, and psoriasis. Axial radiographic features differ between the entities, but Dr. Coates argued differences are driven by HLAB27 status rather than psoriasis. She summarized therapies which have shown to be effective for axSpA, namely TNF, IL-17, and JAK inhibitors. Dr. Coates stated there are currently no adequate disease activity measures for spinal disease and that BASDAS/ASDAS scores, which are used in trials, can change heavily in patients without axial disease because of improvement in their skin, joints, enthesitis, etc. Dr. Coates concluded that although there are some differences, axSpA and axPsA are the same conditions in a spectrum which are being artificially separated based on classification criteria.

Dr. Deodhar opened his argument discussing the advancement of medicine due to the efforts of Drs. Moll and Wright in identifying PsA as a different disease entity rather than 'rheumatoid arthritis with psoriasis'. He then elaborated on the differences between axPsA and axSpA based on demographics, clinical features, and imaging parameters. He also argued that the genetic and biological differences between the two entities with respect to HLAB27 status and IL-17A and IL-17F levels support the concept of the diseases being different disorders. Differences between axPsA and peripheral PsA were also highlighted. Dr. Deodhar concluded that it is important to keep axSpA and axPsA as different entities and that we should keep an open mind about the dynamic/changing nature of diseases, which will help to advance the science of medicine. The debate generated interest and many questions from the audience. We are hopeful that the AXIS and STAR can provide helpful information about axial PsA.

The Axial Involvement in Psoriatic Arthritis (AXIS) Study

Denis Poddubnyy

The AXIS study is a prospective cross-sectional study that has been conducted under the umbrella of ASAS and GRAPPA. The overarching aims of the study are to systematically evaluate clinical and imaging manifestations indicative of axial involvement (based on local and central assessments) in patients with PsA, and to develop classification criteria and a unified nomenclature for axial involvement in PsA that would allow defining a homogeneous subgroup of patients for research.

The study population includes:

- Consecutive patients diagnosed with PsA and fulfilling the CASPAR classification criteria for PsA
- Symptom duration of up to 10 years
- Not receiving b- or ts- disease-modifying antirheumatic drugs (DMARDs) (b- or ts- DMARDs naïve).



Patient enrollment started in four countries in July 2021: USA, Germany, Singapore, and Spain. Thirty-four patients have been enrolled so far (target 400), of which 30 patients have successfully completed eCRF and 12 patients' imaging has been centrally reviewed.

We are awaiting completion of each country's contract and ethical approval procedures so that all centers can start enrolling patients. We thank all participating centers and researchers for their dedication and collaborations!

Clinical and Molecular Characteristics of PsA

Jodi L. Johnson

Dr. Philip Mease presented a project being initiated by GRAPPA's Collaborative Research Network (CRN) to characterize clinical and molecular characteristics of PsA. This project is to be funded by Janssen. Providing biomarkers for the presence of axial involvement in patients with PsA could assist in recognizing these patients sooner, and promoting more targeted assessment and treatment. The study will include a total of 40 patients, 20 with and 20 without evidence of axial involvement. Data will be collected at only one timepoint (baseline). The study plan is to carefully characterize each patient clinically, take blood samples for biomarker analysis in all patients, a stool sample for microbiome analysis, and a punch biopsy from an active skin plaque in 80% of the patients and synovial biopsy in half. Patients on biologics or targeted systemic DMARDs will be excluded, and patients should be within 10 years of PsA diagnosis. Patients will have X-Ray and MRI of the spine and sacroiliac joints. Worldwide sites will accrue patients. Budget and contracts are still being negotiated as well as passing regulatory steps at each of the sites. This is a pilot study to see how the CRN can work together to address important questions for the field.

Guttate Psoriasis

IL-17 vs. IL-23

Our Debatable Understanding of Guttate and Plaque Psoriasis

Sam Hwang, James Krueger, and Kristina Duffin

Guttate psoriasis is believed to be an uncommon variant of plaque psoriasis, accounting for roughly 2-10% of cases. Studies suggest that guttate psoriasis will resolve within a year in the majority (~60%) of patients, but 30-40% may later develop other forms of psoriasis. Underlying causes of guttate psoriasis remain under investigation. While there is a clear association between acute guttate psoriasis and pharyngitis caused by *Streptococcus pyogenes* infection, viruses, including SARS-CoV2 (COVID-19) can also precede development of guttate psoriasis.

Guttate psoriasis is clinically classified as a form of psoriasis, but proteomic profiling in the past has suggested that guttate psoriasis is more similar to contact eczema than psoriasis vulgaris. Dr. Krueger's lab re-examined guttate psoriasis using gene expression profiling (Affymetrix U133 2.0Plus arrays and RT-PCR). Results using gene set enrichment scores showed that guttate psoriasis is more similar to psoriasis vulgaris than to various forms of eczema. Expression of the central IL-23/Type 17 T-cell pathway and a higher expression of regulatory immune pathways were found in guttate psoriasis. This suggests the potential for long-term disease clearing if treated with targeted therapeutics.

To date, the standard of care of guttate psoriasis includes topical agents for less severe cases, and phototherapy or systemic agents for moderate-severe cases. Although "dogma" suggests that antibiotics for Streptococcal infection may be helpful, a past Cochrane review did not support antibiotic use for guttate flares. Small observational studies suggest that biologics that target IL-12/23, IL-23, and IL-17 are effective and may induce long-term remission. Randomized control trials of interventional drugs are needed to assess best treatments for this condition, but trial design is challenged by the uncommon nature of the outbreaks, spontaneous remission, lack of validated endpoints, and the need for long-term follow up.



Debate: Targeting IL-23 vs. IL-17

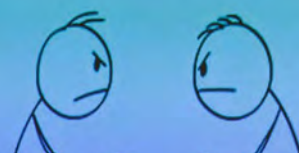
Guilherme Muzy

Following the 2021 debate on which treatment strategy would be better suited for patients with moderate-to-severe psoriasis and mild PsA, targeting IL-23 or IL-17, Dr. Armstrong and Dr. Merola explored the plethora of data available to dermatologists and rheumatologists on the topic.

Dr. Armstrong started the debate presenting the robust, high-quality data showing that IL-17i ixekizumab and secukinumab inhibit radiographic progression of PsA. She then argued that IL-17 inhibition appears to work well on oligoarticular and subclinical disease, as demonstrated by the IVEPSA study with secukinumab. IL-23 inhibition does not have the same robust level of data.

Dr. Merola then argued for the data behind IL-23 inhibition, including the advantage of fewer injections compared to IL-17 inhibition, increasing patient satisfaction and adherence. There has been proven efficacy in IL-23 inhibition of PsA with very high rates of sustained responses for both guselkumab and risankizumab compared to secukinumab. The potential mechanistic benefits of IL-23 inhibition leading to disease modification were shown through greater suppression of CD8 + Tissue Resident Memory cells in patients treated with guselkumab compared with secukinumab. Dr. Merola also presented recent data on the impact of guselkumab on axial disease symptoms as we await data of on-going studies in both axial disease and for inhibition of radiographic progression. He summarized by saying IL-23 inhibition represents a potentially ideal intervention to maximize efficacy, safety, durability, rapidity of onset, and low burden on both patients and clinics (with infrequent dosing, minimal monitoring, and excellent availability in the US).

IL23 vs. IL17 in moderate to severe psoriasis with mild psoriatic arthritis: the debate



COVID - Global Perspective

Risk Factors for Severe COVID-19 Outcomes: Immune-mediated Inflammatory Diseases, Therapies, and Comorbidities in a Large US Healthcare System.

Jodi L. Johnson

Dr. Philip Mease summarized a large statistical and machine modeling study on risk factors for severe COVID-19 outcomes in patients with immune mediated inflammatory diseases (IMIDs) using data from the Providence St. Joseph US healthcare system which includes 51 hospitals and nine million patients, of which 270,000 had IMIDs. Before the Omicron variant (March 1, 2020 to December 25, 2021) there were 162,746 patients diagnosed with COVID-19, of which 6185 had IMIDs. Of those with IMIDs, 3% were hospitalized and 4.5% died as opposed to those without IMIDs where 2.4% were hospitalized and 3.1% died. After Omicron became the predominant variant (December 26, 2021 to April 13, 2022) 68,0927 patients were diagnosed with COVID-19 and again the number of IMID patients who were hospitalized (1.5%) and died (3.2%) were higher than those without IMID (0.7% hospitalized, 1.7% died). Multivariable logistic regression analysis showed that increasing age and comorbidities associated with more hospitalization and death while being vaccinated and boosted associated with less hospitalization and death. Type of IMID and treatment were not significantly associated with risk of hospitalization or death pre-Omicron, but post-Omicron, spondyloarthritis and Sjogren's syndrome as well as TNFi use associated with lower risk of hospitalization and death. Machine learning models confirmed that age and comorbidities were the greatest risk factors for severe outcomes and vaccination was protective. Importantly, neither psoriasis nor PsA nor their therapies were associated with increased risk for severe outcomes.

Anti-virals and Immunocompromised Patients – What Should You Know?

Jodi L. Johnson

Peter Nash presented on considerations for use of anti-viral therapies in immunocompromised patients. Statistics show higher risk of severe outcomes in patients with IMIDs. The presentation covered considerations for oral anti-virals molnupiravir (Lagevrio) and nirmatrelvir (Paxlovid), intramuscular (IM) prophylactic treatment tixagevimab/cilgavimab (Evusheld), and intra-venous (IV) treatments sotrovimab (Xevudy) and remdesivir (Veklury). Drug interactions between some of these medications and immunomodulatory medications, particularly Paxlovid, are of concern and should be closely examined. The "Covid-19" iPhone app from University of Liverpool is particularly helpful for assessing drug interaction risks. Some patients at high risk for hospitalization and death, especially those on rituximab with poor vaccine response can receive prophylactic IM treatment. A small study indicated that there is an advantage to prophylactically treating these patients using tixagevimab/cilgavimab. Remdesivir reduces time to recovery but does not offer significant effect on survival. Recommendations are to use monoclonal antibodies plus Paxlovid for B cell depleted patients with COVID-19 and for others to just use Paxlovid. If drug interactions are of concern, consider molnupiravir.

Immunity After SARS-CoV-2 mRNA Vaccines in Patients with Immune Mediated Inflammatory Disease (IMID)

Vinod Chandran

We investigated antibody and T cell responses and durability of SARS-CoV-2 mRNA vaccines (BNT162b and/or mRNA 1273) in IMID patients on immunomodulatory therapy other than B-cell depleting therapy and corticosteroids. We prospectively examined vaccine response in 150 adult patients with IMIDs (psoriatic disease, axial spondyloarthritis, inflammatory bowel disease, and rheumatoid arthritis) with or without maintenance therapies (TNFi, methotrexate/azathioprine [MTX/AZA], TNFi + MTX/AZA, IL-12/23, IL-17, and IL-23 inhibitors) compared to healthy controls. Four timepoints were analyzed using ELISA for IgGs to COVID spike trimer, the spike receptor binding domain, and the nucleocapsid protein (NP). T-cell release of cytokines (IFN gamma, IL-2, IL-4, IL-17A, TNF) and cytotoxic molecules (sFasL, Gzma, Gzmb, Perforin) was analyzed in cell culture supernatants following stimulation with spike or NP. The 4 time points were T1=pre vaccination, T2=median 26 days after vaccine dose 1, T3=median 16 days after vaccine dose 2 and T4=median 106 days after vaccine dose 2. We observed that most patients mounted antibody and T cell responses with increases from dose 1 to dose 2 (100% seroconversion at T3) with some decline in these responses by T4. Antibody levels and neutralization efficacy was lower in TNFi groups compared to controls and waned by T4. These findings highlight the need for a third vaccine dose in patients undergoing treatment with TNFi.

Patient Research Partners Provide Patient Perspectives on COVID-19 and Psoriasis

Suzanne Grieb

To provide patient perspectives to the GRAPPA 2022 COVID-19 panel, the Patient Research Partners (PRP) anonymously responded to several open-ended questions through a Qualtrics form. These questions allowed the PRPs to share aspects of their experiences during the pandemic as well as continued concerns and desires. Three key findings were shared during the panel:

- 1) The pandemic has been a challenge to several PRP's mental wellbeing. The prevalence of depression among people living with PsA is higher than the general population and so it is important that providers begin to, or continue to, make discussion about mental wellbeing part of disease care.
- 2) Lingering concerns about COVID-19 and PsA care center on medications. For example, are patients more vulnerable to COVID infection around the time of an injection? If a patient gets infected with COVID-19, will the medication impact the course of COVID disease (should the patient continue with their medication)?
- 3) The patients' personal providers (and their clinics) are the most trusted source of information related to the pandemic and PsA. There is a desire for more proactive communication about new research findings and their implications for PsA patients from their doctors or clinics (i.e., a monthly email or newsletter).

Diversity, Equity, and Inclusion

Diversity, Equity, and Inclusion—My Perspective

Niti Goel

Personal biases and those of others need to be systematically removed to ensure diversity, equity, and inclusion (DEI) in healthcare delivery and research. Each person is different but often identifies in many ways. For example, depending on the moment, I identify as a woman, Asian, mother, wife, rheumatologist, person with psoriatic disease, United States-born, and GRAPPA patient research partner. To respect diversity, we need to remember that disease presentations vary between each person, and available treatments may not always work. For example, when examining the impact of sex on PsA, there is evidence that women compared to men might have more disease activity, different disease manifestations, and worse outcomes. Further, women have reported they have been discriminated against due to their sex when receiving healthcare. To address DEI to allow for personalized treatment, at a minimum, we all have a responsibility to ensure that clinical studies include diverse individuals, that results are routinely reported for different aspects of diversity, and that healthcare delivery is optimized for people from all backgrounds.

Sex- And Gender-based analysis of Effectiveness of advanced therapies in Psoriatic Arthritis (SAGE-PsA)

Lihi Eder

While PsA is distributed equally in men and women, the condition affects them in very different ways. Women living with PsA are less likely to achieve remission and tend to discontinue treatments earlier than men. Little attention has yet been given to understanding which sex- and gender-related mechanisms explain these disparities. SAGE-PsA is a GRAPPA endorsed study that aims to fill some of these gaps in knowledge.

By viewing the data according to sex and gender, we aim to uncover mechanisms underlying these disparities. We plan a prospective, multicenter study involving 30 sites that represent high- and middle-income countries.

Patients with PsA who will begin treatment with one of the four classes of advanced therapies will be enrolled. Patients will be evaluated before and after initiating therapy to assess their response. To separate the effects of sex and gender, we will consider attributes that represent both constructs in statistical analyses. We will also assess whether age and ethnicity intersect with gender in terms of treatment response.

We are currently securing funding for this study. A survey was sent to GRAPPA members inviting interested sites to apply for participation. We anticipate starting recruitment for this study in 2023.

Race, Ethnicity, Sex and Gender in research

Alaina J James

Definitions

Race: a classification of people based on phenotypic characteristics; defined and often assigned by the dominant group to maintain systems of power (Holocaust, Slavery, Caste)

Ethnicity: membership in a group with shared culture, tradition, language, religion and/or geographic area (Latino/a/x, Hispanic)

Sex: genetic and biologic (sex karyotype with female, male, intersex)

Gender: behaviors, dress, mannerisms, roles, and relationships associated with an individual's sex and identity (social differences between female and male/feminine or masculine). Gender definitions vary from society to society and can change over time.

Race and ethnicity are social constructs, without scientific or biological meaning. Hence, reporting race and ethnicity (social identities) with sociodemographic factors and social determinants is appropriate. Research studies should report the source (self-identified or record) of the racial/ethnic classification and reasons for reporting these. Neglecting to report race and ethnicity in health research may conceal health disparities and inequities. The wording is important and specific racial and ethnic categories are preferred over collective terms like Other, Non-White, Minorities, BIPOC, BAME, SOC. When reporting race and ethnicity, list the categories in alphabetical order in text and tables.

Gender is also a social construct, while sex is genetic and biologic. The Sex and Gender equity in Research recommendations are:

- Report sex assigned/identified at birth and gender identity.
- Report source of information: (participant, physical exam, genetic tests).
- Determine differences based on genes, sex hormones, and/or societal stratification.



Diversity, Equity, and Inclusion



Sex and Gender in PsA and Spondyloarthritis (SpA): Existing Gaps

Jodi L. Johnson, PhD

Irene van der Horst-Bruinsma presented on sex and gender differences in SpA and PsA. For Ankylosing Spondylitis (AxSpA) the incidence ratio is 70% men to 30% women with men being diagnosed younger than women. Women often experience longer delays in diagnosis and have higher BASDAI and BASFI scores and more peripheral joint complaints, while men tend to have higher CRP and higher radiographic progression. ASDAS scores are roughly the same between men and women.

For PsA the incidence ratio men:women is 50:50 with no differences in onset or time of diagnosis. Women have higher BASDAI, HAQ, and pain scores. Men have higher skin involvement with greater PASI and BSA, more nail involvement, and greater axial involvement. Women have more tender and swollen joints as well as higher enthesitis scores.

Acknowledging and continuing to learn about health disparities between men and women with regard to SpA and PsA is clinically important, particularly when studying treatments. Drugs are often tested pre-clinically in male mice and in early clinical trials in healthy men. There are usually no dosage corrections for body weight and gender – doses are typically calculated from a normal male of 70kg. There is also no gender correction in post-marketing studies. Work is being done to include more healthy females in clinical trials.

A pooled data study was done looking at sex and gender differences in men and women using etanercept to treat SpA (n=1283) patients. Patients were stratified by gender and observed for baseline characteristics, drug efficacy, and discontinuation rates after 12 weeks. Findings were that ASDAS scores improved more significantly in males than females. Another study found that male patients on TNF inhibitors responded better than female patients at one and two year follow-up. A larger study confirmed these data and added that women were more likely to discontinue taking TNFi. Differences between sexes in patients taking IL-17 inhibitors were lower than with TNFi but did slightly favor greater efficacy in males.

When looking at data from PsA patients, female patients also showed a lower response rate to TNFi compared to male patients, had higher disease activity scores, and higher discontinuation rates. Females have a higher burden of PsA after ustekinumab or TNFi treatment and are more likely to discontinue treatment. Much work remains to be done to learn about and correct for gaps between men and women SpA and PsA patients.

Group Reports

Collaborative Research Network (CRN)

Vinod Chandran and Kurt de Vlam

The GRAPPA CRN and Research Committee (RC) co-chairs, Vinod Chandran and Kurt de Vlam, held an informative meeting just after the annual GRAPPA meeting ended. There is an ongoing organizational reform of GRAPPA where the CRN will be integrated into the more global RC. In the coming months plans will be developed for integrating the CRN, working with research special interest groups within the RC, and updating the composition of the RC. Rules for grant applications will be modified and an agenda for the next three years will be developed in consultation with the new members of the RC. A proposal of a GRAPPA young investigator fellowship will be studied and proposed to the Executive Committee. The status of the various projects were then reviewed including the GRAPPA-Atturo-Pfizer (PsA BioDAM), GRAPPA-Atturo-Lilly, GRAPPA J&J- Clinical and Molecular Characterization of Axial Psoriatic Arthritis study, AXIS and the Hippocrates Project, and an IMI (European industry and academia sponsored) biomarker study in which GRAPPA is a partner. The meeting concluded with a talk by Dr. Schett on academia-industry partnership.



International Dermatology Outcome Measures (IDEOM) at GRAPPA

Melissa Peri Zundell and Jenna Yousif

Dr. Alice Gottlieb introduced IDEOM by underscoring the organization's mission to enhance both the research and treatment of those with dermatologic disease through patient centered measurements. Select ongoing projects in the Psoriatic Disease workgroup were highlighted.

Measuring Musculoskeletal (MSK) Symptoms in Psoriasis Studies:

Dr. Joseph Merola presented an update on behalf of the MSK Symptoms Working Group and the IDEOM MSK instrument for the detection of pre-PsA (psoriatic arthritis), early PsA, and undiagnosed PsA. Dr. Lourdes Perez-Chada elaborated on the instrument's development based on the COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) methodology. After several rounds of pilot testing and modifications, the current version is a nine-item questionnaire divided into three sub-scales and aims to measure the intensity and impact of MSK symptoms on health-related quality of life. Following steps include field-testing, further validation, and use in clinical studies.

Integration of the Psoriasis Epidemiology Screening Tool (PEST) and Psoriatic Arthritis Impact of Disease (PsAID) into EPIC:

Dr. Alice Gottlieb presented an update on the integration of the PEST and PsAID questionnaires into EPIC. Patients will complete the PEST and PsAID (both available free on the GRAPPA app) before meeting with their healthcare provider to assist in the detection of undiagnosed and undertreated PsA.

Treatment Satisfaction:

Dr. April Armstrong presented an update on the IDEOM DermSat-7 treatment satisfaction instrument for psoriasis that is currently under evaluation via a multi-center cross sectional validation study. Within the conceptual treatment satisfaction framework, the three domains of focus are effectiveness, convenience, and adverse events. Dr. Vibeke Strand presented on the rationale behind seeking treatment satisfaction among patients with psoriasis and PsA and the need to refine terminology to make these instruments more user-friendly.



Group Reports

The GRAPPA-OMERACT Outcome Measure Group Report

Katy Leung, William Tillett, Maarten de Wit and Dafna Gladman

Since completing the aim to update and endorse the core domain set for PsA in 2016, the GRAPPA-Outcome Measure in Rheumatology Outcome Measure Group is now using the OMERACT framework to appraise and endorse the core outcome measurements for each domain. The working group focused on composite measures this year. Composite measures enable the combination of numerous domains that are equally important into a single measure, giving an estimate of total disease burden. They are used in rheumatology to measure disease activity and are often the primary or key secondary outcomes in clinical trials.

Despite advances in treatment options, many of the clinical trials in PsA are still using composite outcomes developed for other rheumatic conditions (e.g. rheumatoid arthritis, axial spondyloarthritis) as the primary endpoint. The Outcome Measure Group is appraising and evaluating the measurement properties of composite outcomes that were developed in recent years specifically for PsA. The OMERACT composite group intends to prioritize instruments based on their clinical merit rather than instruments with the most historic data, which tends to prioritize older measures that have had more opportunity than the newer measures to be tested.

Outcome measures should be evaluated in a well-defined population, and for a well characterized intended purpose of use. Concerns have been consistently raised about important measures to patients that may not be adequately reflected in existing composite measures. To address these concerns the working group is engaging patients in the appraisal process. Patient perspectives are particularly relevant for establishing content validity, the feasibility of the measure tool, and the response options of an instrument.

After a few rounds of discussion and voting, the composite working group has narrowed the number of promising composite measures. These include the ACR20/50/70 responses, Minimal Disease Activity (MDA), Disease activity index for PsA (DAPSA) and Psoriatic Arthritis Disease Activity Score (PASDAS). Other composite measures are still being considered. A survey will be sent to all GRAPPA members about which composite outcomes should be taken forward for further evaluation.

Patient Research Partner Network Report

Ingrid Steinkoenig

The GRAPPA Patient Research Partner (PRP) Network currently has twelve dedicated patient members from seven countries with various backgrounds and careers who work to support the physicians, researchers, and scientists of the greater GRAPPA community. Many patient members are also patient advocates in other groups such as OMERACT, EULAR, EULAR-PARE, IDEOM, NPF, ICHOM, HKPsAA, FOREUM, etc. as well as participating in local patient groups. We are organized under our own developed Procedures and Policies which mirror and support the GRAPPA mission at large. We participate in most GRAPPA committees including GRAPPA-EU.

GRAPPA's PRP Network provides the patient voice to numerous GRAPPA projects including the GRAPPA Treatment Recommendations 2021 Update, Informatree (.org), the Innovative Medicines Initiative (HIPPOCRATES), the Pfizer/GRAPPA Educational Series of 2021/2022 (CAPES, and other educational projects), the SAGE-PsA study, DUET study, DEPAR study, GRAPPA/ASAS Axis study, AxPsA study, GRAPPA-OMERACT working group, CRN working group, and the GRAPPA- UCB Medical Education Taskforce.

In addition to continuing our work on GRAPPA studies and projects, we will update our governance and the popular accompanying PRP Handbook. One of our immediate goals is creating more diversity (in all aspects) within our network to better represent the global perspective of patients living with psoriatic disease.

We are keen to develop a working relationship with Y-GRAPPA in areas yet to be identified. Please contact our Chair and Chair-elect if you are interested in a specific collaboration with one or more of our PRP Network members.



Trainee Symposium



Development of a Biologic Treatment Decision Algorithm According to the Peripheral T-Helper Cell Profile using a Cytokine Secretion Assay: A Proof of Concept Study

Gizem Ayan

Recent studies have shown that peripheral T-cell profiling is helpful in treatment decision making for PsA. We aimed to develop a treatment decision algorithm based on a T-cell cytokine secretion assay in real-time that can be implemented in daily clinical practice. To this proof-of-concept analysis, newly diagnosed PsA patients who met CASPAR criteria and who are either csDMARD or bDMARD naïve were included. Immunophenotype analysis was done using anti-human-CD3, CD4, and CD8 markers and a cytokine-secretion assay (IFN- γ , TNF- α , IL-22 and IL-17). The algorithm was developed using all patients' results. Ratios of IFN- γ , TNF- α , IL-22 and IL-17 cytokines specific to CD4+ and CD8+ cells were calculated. Cut-off values for the algorithm were determined from the median of ratios; 1) CD4+ TNF- α /IFN γ ; 2) CD8+ TNF- α /IFN- γ ; 3) CD4+ IL-22 and IL-17. Overall, 19 patients (n=8 initiated csDMARD, n=11 initiated bDMARD) were included with the mean age of 45 years. Using predefined cut-off values the real-time algorithm was developed using a precise functional assay showing exact T-cell behavior compared to the previous assessments that had only analyzed cellular phenotype and that only provided results 24h after blood taking.

Neural networks to discriminate between RA and PsA

David Simon

We investigated whether neural networks can discriminate between seropositive RA, seronegative RA and PsA based on inflammatory patterns from MRI and tested how psoriasis patients without any clinical signs of arthritis fit into such patterns. MRI scans from 649 patients (135 seronegative RA, 190 seropositive RA, 177 PsA, 147 psoriasis) were fed into ResNet neural networks. The area under the receiver operating characteristics curve (AUROC) was 75% for seropositive RA versus PsA, 74% for seronegative RA versus PsA and 67% for seropositive versus seronegative RA. All MRI sequences were relevant for classification, but there was little loss of power when contrast agent-based sequences were excluded. Adding demographic and clinical data to the networks did not significantly improve classification. The neural networks mostly assigned psoriasis patients to PsA, suggesting that a PsA-like MRI pattern may be present early in the course of psoriatic disease. Neural networks can be successfully trained to discriminate MRI inflammation associated with seropositive RA, seronegative RA, and PsA.

Challenges regarding the treatment of PsA in Latin America

André Ribeiro.

PsA presents differently in Latin America and its treatment is hindered by several aspects of care that are specific to this region of the globe. A systematic literature review was performed to map the challenges described in the literature, with inclusion of 15 articles after searching PubMed, EMBASE, and LiLacs. There were nine main categories of difficulties identified. The incidence of opportunistic infections, mainly tuberculosis, was the most common. In addition, many studies reported difficulties regarding logistics such as limited access to rheumatologists and medications as well as difficulties regarding dispensation and home-storage of disease-modifying antirheumatic drugs. This systematic literature review highlights the importance of:

Caring for the patient as a whole

Remembering the importance of infectious complications

Focusing on logistics

Educating patients

A survey of rheumatologists and patients from different settings will be administered to assess whether the challenges identified in the present work truly represent the reality in Latin America.

Trainee Symposium

Treat-to-target dose reduction and withdrawal strategy of TNF inhibitors in Psoriatic Arthritis and Axial Spondyloarthritis: a randomized controlled non-inferiority trial

Celia A.J. Michielsens

TNFis are effective in PsA and axSpA but have disadvantages which could be ameliorated by treat-to-target (T2T) tapering strategies. We performed an open-label, monocenter, randomized, controlled non-inferiority (NI) trial on TNFi T2T tapering strategies. PsA and axSpA patients using a TNFi with ≥ 6 months stable low disease activity (LDA) were randomized to a T2T tapering or no-tapering strategy, and followed-up for 12 months. Tapering consisted of 3-monthly tapering steps (66%, 50%, 0%), with re-intensification in case of flare. The primary endpoint was the difference in proportion of patients having LDA at 12 months, with a NI margin of 20%. We included 122 patients (n=81 tapering (PsA, n=42, axSpA, n=39)). The proportion of patients in LDA at 12 months for the tapering and no-tapering group was 69% and 73%: adjusted difference 5% (Bayesian 95% credible interval: -10% to 19%), confirming NI. The mean percentage Daily Defined Dose (%DDD) was respectively 53% and 91% at month 12. In conclusion, a T2T TNFi strategy with tapering is non-inferior to a T2T strategy without tapering regarding the proportion of patients in LDA at 12 months, resulting in a substantial reduction of TNFi use.



Screening for the Early Identification of Psoriatic Arthritis with Axial Involvement (axPsA) in a Cohort of Italian Patients Affected by Psoriasis: Preliminary Results of a Dermo-Rheumatologic Cross-Sectional Study (ATTRACT)

Devis Benfaremo

There is growing interest in early identification of patients with axial PsA (AxPsA) to allow better disease characterization and well-timed, targeted therapeutic strategies. In this study, we screened consecutive patients with psoriasis, excluding those treated within 12 weeks prior to screening with any conventional or biologic DMARD, using a Dermatologic-Centered Screening (DCS) tool questionnaire. Patients who positively responded to both of two entry questions regarding back pain features (duration >3 months and age of onset <45 years) plus at least one additional secondary question were considered primarily eligible for rheumatologic evaluation (Figure. 1).

From February 15th to May 31th, 236 patients were screened. A total of 103 patients (43.6%) answered yes to both entry questions, 88 patients (37.3%) were considered non-eligible for rheumatologic evaluation, and 45 (19.1%) answered yes to only one of the entry questions. Patients eligible for rheumatologic evaluation were more likely to be female and younger than those not eligible. To date, 11 patients (10.7%) have already been classified as having AxPsA (9 of them fulfilling ASAS criteria and 9 also affected by peripheral disease).

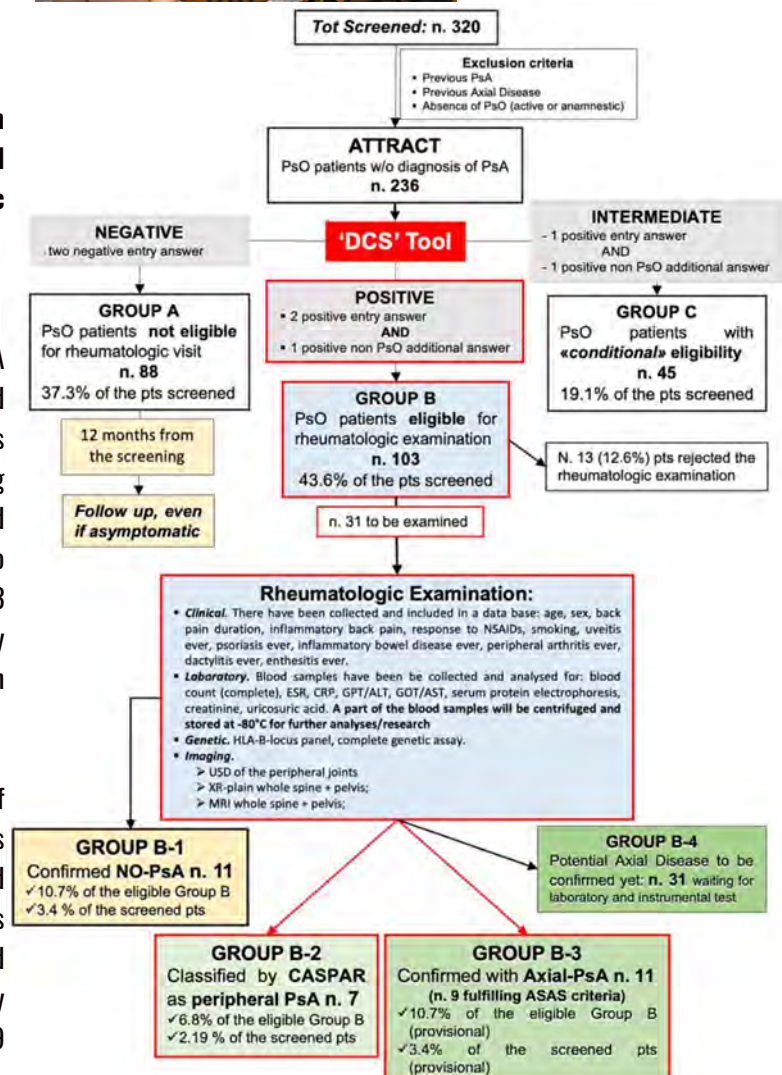


Figure 1. Flow-chart of the ATTRACT (Axial psoriaTic arThritis scReening AnCona iTaly) study. DCS: Dermatologic-Centered Screening tool.

GRAPPA - Credits



We thank the following committee members for their years of service:

Alice Gottlieb
Elaine Husni
Peter Nash
Jose Scher
Alexis Ogdie

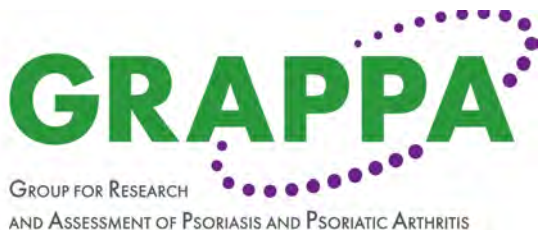
We welcome the following elected committee members:

Steering Committee:

Ennio Lubrano, Rheumatologist, Italy (Re-elected)
Laura Coates, Rheumatologist, UK
Lourdes Perez-Chada, Dermatologist, USA
Maria Antonietta D'Agostino, Rheumatologist, Italy
Sam Hwang, Dermatologist, USA
Stephen Pennington, Scientist, Ireland

Executive Committee:

Vinod Chandran, Rheumatologist, Canada (Re-elected)



GRAPPA Executive Committee 2022



SAVE THE DATE
GRAPPA 2023 Annual Meeting and Trainee Symposium
July 13-15, 2023
Dublin, Ireland