














GRAPPA 2023: Major Projects, Key Advances, and Milestones

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ABSTRACT. At the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) 2023 annual meeting, members were updated on a number of ongoing activities during the key project update session. These activities included the Axial Involvement in Psoriatic Arthritis (AXIS) cohort, the Axial Psoriatic Arthritis Molecular and Clinical Characterization study, the Diagnostic Ultrasound Enthesitis Tool (DUET) study, the Sex- and Gender-Based Analysis of the Effectiveness of Advanced Therapies in Psoriatic Arthritis (SAGE-PsA) study, the Health Initiatives in Psoriasis and Psoriatic Arthritis Consortium European States (HIPPOCRATES), the GRAPPA slide library, and the GRAPPA treatment recommendations.

Key Indexing Terms: education, GRAPPA, project, psoriasis, psoriatic arthritis, research

Introduction

Over the years, the Group for Research and Assessment in Psoriasis and Psoriatic Arthritis (GRAPPA) has demonstrated a strong focus on research and education. In particular, research activities through the establishment of the GRAPPA Collaborative Research Network (CRN) and the research committee have led to major advances in the field of psoriatic disease (PsD), including patient care.¹ GRAPPA is also making a significant contribution to education, offering global seminars through virtual platforms and developing its international presence through educational sessions at major events. Online educational resources are being created for both patients and health professionals.² At this year's annual meeting, members were updated on the milestones of key projects in line with

GRAPPA's mission. These included the Axial Involvement in Psoriatic Arthritis (AXIS) cohort and the Axial Psoriatic Arthritis Molecular and Clinical Characterization studies, which will provide important information on the definition/criteria of axial psoriatic arthritis (axPsA) and on the molecular etiopathogenesis of axial involvement. Additional research projects discussed were the Diagnostic Ultrasound Enthesitis Tool (DUET) study, which aims to develop a new sonographic scoring system for enthesitis, and the Sex- and Gender-Based Analysis of the Effectiveness of Advanced Therapies in Psoriatic Arthritis (SAGE-PsA) study, which aims to investigate how sex and gender influence the treatment response in PsA. The session also highlighted the significant progress being made by Health Initiatives in Psoriasis and Psoriatic Arthritis Consortium

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European States (HIPPOCRATES) in addressing key challenges in PsD, including the identification of risk factors for PsA through a prospective observational study. From an educational perspective, the GRAPPA slide library was launched, which is an evolving collection of educational slides, with future plans for translations and updates. Finally, as a very important aspect of the contribution of GRAPPA to patient care in PsD, the latest progress in treatment recommendations was presented, with plans for the next update in 2024.

AXIS cohort, by Dr. Dafna Gladman

The AXIS cohort is a joint initiative of the Assessment of Spondyloarthritis international Society (ASAS) and GRAPPA. Dr. Gladman presented an update on behalf of herself and Dr. Denis Poddubnyy, co-principal investigators of the study. The objectives are (1) to determine the frequency of axial involvement in patients with PsA (based on the local and central assessments), (2) to identify the frequency of active inflammatory and structural changes on imaging suggestive of inflammatory involvement of the axial skeleton in PsA, and (3) to identify factors (clinical, lab, imaging) associated with the presence of axial involvement in PsA (determined based on local and central assessments).

The study is designed as a multicenter global study of consecutive patients with PsA according to Classification for Psoriatic Arthritis (CASPAR) criteria, with symptom duration of less than 10 years and not receiving biologic or targeted synthetic disease-modifying antirheumatic drugs. Each patient undergoes a complete history and physical examination as well as imaging of the spine and sacroiliac joint, both by radiography and magnetic resonance imaging (MRI). The imaging is reviewed by both the local investigator and a central imaging committee. The local investigator provides their assessment of the presence of axial disease, whereas the central imaging committee reviews both clinical and imaging results.

By the time of the GRAPPA 2023 annual meeting, 294 patients from 16 countries and 32 centers (recruiting < 10 patients: Brazil, Lebanon, Canada, Argentina, Romania, Mexico; recruiting 10-20 patients: India, Singapore, Hong Kong, Taiwan, South Africa; recruiting 20-30 patients: Italy; recruiting 30-40 patients: USA, Spain; recruiting 40-50 patients: Germany, UK) had been included (Figure 1). Recruitment was expected to be completed by the end of 2023, followed by data cleaning with some preliminary results expected in early 2024.

Axial Psoriatic Arthritis Molecular and Clinical Characterization study, by Dr. Philip Mease

Dr. Mease presented an update on the GRAPPA CRN project, known as the Axial Psoriatic Arthritis Molecular and Clinical Characterization study, an independent investigator study sponsored by Janssen. The primary goal of the project is to identify liquid and/or tissue biomarkers to help distinguish the presence of axial involvement in PsA. A secondary goal is to do the first “trial run” of a CRN-managed clinical and translational science study, enrolling patients from multiple centers and determining the infrastructural competence to perform the complex logistics

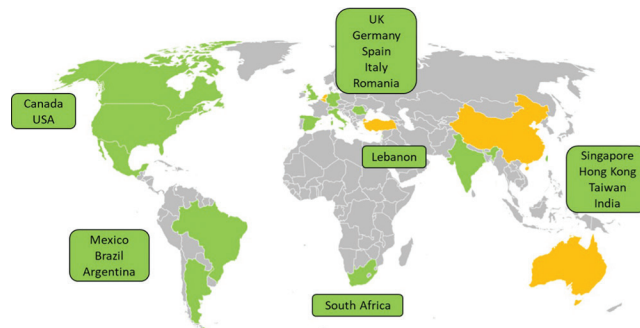


Figure 1. AXIS cohort global representation by July 2023. Countries in green represent the active centers, whereas countries in yellow are pending procedures to be activated. AXIS: Axial Involvement in Psoriatic Arthritis.

of multisite project design, ethics approval, site coordination, sending blood and tissue across borders, capturing electronic data centrally, and handling finances. We plan to enroll 40 biologic-naïve patients with PsA with disease duration less than 10 years, half with and half without axial involvement; collect clinical data; and send blood, stool, skin, and synovial biopsy samples to the University of Toronto (Dr. Vinod Chandran) as the central repository. Imaging, radiography, and MRI of sacroiliac joints and spine will be read centrally. Extensive biomarker analysis is planned. Project leads are Drs. Mease, Oliver FitzGerald, and Chandran. The study coordinator is Dr. Melissa McIlraith. The Mease site has completed enrollment of the first 5 patients. Six other global sites are proceeding through contractual and regulatory processes, with plans to complete study enrollment during 2024.

DUET, by Drs. Lih Eder, Sibel Aydin, and Gurjit Kaeley

Enthesitis is a key feature in PsA and may be the initial site of musculoskeletal inflammation in patients with PsA. The DUET study aims to develop a new sonographic enthesitis scoring system to improve early diagnosis of PsA. The study, led by Drs. Eder, Aydin, and Kaeley, started as a GRAPPA project in March 2021 and completed enrollment at 17 sites from 8 countries in March 2023. The study included a prospective collection of data from rheumatologist assessment, patient surveys, and ultrasound (US) scanning of 16 enthesal sites. All US scans were scored for inflammatory and structural enthesal lesions by 3 central sonographers. The study enrolled a total of 215 patients with PsA, 100 patients with psoriasis (PsO) alone, and 106 nonpsoriatic controls. Preliminary results presented at the GRAPPA 2023 annual meeting showed a high prevalence of tender entheses among all participants, including the control patients, which suggests that clinical diagnosis of enthesitis lacks specificity. Some enthesal sites were more tender than other sites across all patient groups. A strong correlation was found between clinical enthesitis score contextual factors, such as age, sex, and BMI. Clinical enthesitis score also correlated with high scores in “pain-sensitive” domains. The team currently works on analyzing the US data with the aim to develop a new diagnostic sonographic system to improve diagnosis of PsA.

SAGE-PsA, by Dr. Lihi Eder

SAGE-PsA is an international, multicenter study supported by GRAPPA through multiple pharmaceutical industry-supported grants. The study aims to understand how sex and gender influence response to advanced therapies in PsA; specifically, it aims to determine what biological and sociocultural mechanisms explain the differences in treatment response between men and women with PsA.

SAGE-PsA involves 36 sites from 18 countries, led by GRAPPA members. The study will enroll 540 men and women with active PsA who are starting treatment with advanced therapies and follow them for up to 1 year. In addition to a comprehensive assessment of PsA disease activity, the study will collect information to allow better understanding of the role of sex- and gender-related mechanisms as determinants of treatment response. Such mechanisms include comorbidities, sex hormones, immune profile, pain mechanisms, gender-related sociocultural factors, and more. SAGE-PsA was launched in March 2023 and has enrolled 27 patients to date. The team planned to activate all participating sites by the end of 2023 and complete study enrollment by 2025.

SAGE-PsA should improve our understanding of the effects of sex and gender on PsA, which will contribute to more personalized approaches to caring for people living with PsA.

HIPPOCRATES consortium update, by Drs. Oliver FitzGerald and Stephen Pennington, on behalf of the HIPPOCRATES consortium

HIPPOCRATES is a large Innovative Medicines Initiative-funded European consortium focused on addressing unmet needs in PsD (<https://www.hippocrates-imi.eu/>). In total, there are 27 partners including academic institutions, pharmaceutical companies, small-medium sized enterprises, and patient representative organizations. The total budget for the 5-year project is €22.5 million, and the project began in 2021. The following 4 areas of unmet need are the focus of 4 of the 8 project work packages (WPs): (1) the development of a diagnostic test or algorithm for PsA, (2) the identification of risk factors that identify which patients with skin PsO will develop PsA, (3) an understanding of the clinical or molecular factors that contribute to joint damage, and (4) the development of a precision medicine approach to treatment.

Since the project commenced, there have been several areas of progress, including the following: (1) WPs and working groups are all established and functioning well; (2) extensive sample

cohorts have been identified and prioritized; (3) a consortium-wide material transfer agreement and a data sharing agreement have been agreed and signed-off by all partners; (4) a pilot multiomic study has been completed using shared samples from a small cohort of patients with either skin PsO and no musculoskeletal involvement or established PsA; (5) there have been multiple meeting abstracts, posters, and publications; and (6) the HIPPOCRATES Prospective Observational Study (<https://hpos.study>), which aims to recruit and follow 25,000 people with cutaneous PsO to identify risk factors for the development of PsA, has been launched (Figure 2). Now that the project's administrative structures and agreements have been established, it is anticipated that this will pave the way for substantial progress in addressing the key unmet needs in PsA for the benefit of patients.

GRAPPA slide library update, by Drs. Gizem Ayan, Fabian Proft, and Philip Helliwell

The project to update the GRAPPA slide library was launched in March 2022, with the support of the GRAPPA education committee and a dedicated team of GRAPPA experts under the leadership of Drs. Helliwell, Janine Kowack, Proft, and Ayan.

The project started with a call for participation to identify enthusiastic Young-GRAPPA members to work on the update. The project soon gained momentum, and experienced senior members were invited to partner with junior colleagues. Individual teams were formed for each of the 11 slide decks found in the Table. A key step in this endeavor was the development of standard operating procedures (SOPs) and a template for the slides. These guidelines streamlined the use of existing slides and the strategy for creating new slides, and emphasized thorough referencing and copyright compliance.

Teams began working on creating the new decks in May 2022. The first draft of each deck was checked to ensure that the SOPs were followed. Copyright holders were then contacted, permissions were obtained, and any necessary copyright payments were made.

A systematic review process was then created to ensure the quality and accuracy of the slide library update. A panel of reviewers was drawn from the team, wherein reviewers were those specifically not involved in creating the respective deck being reviewed. Reviewers followed a structured template consisting of 4 key questions to standardize their reviews. Individual teams worked diligently on multiple reviews; final versions were reviewed by Annie Spangler to make the decks more visually appealing. Each deck was then submitted to the GRAPPA slide library website. A summary of the procedures can be found in Figure 3.

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"Any dissemination of results must indicate that it reflects only the author's view and that the JU is not responsible for any use that may be made of the information it contains."

Figure 2. Administrative structure and agreements for the HIPPOCRATES Prospective Observational Study. Retrieved from <https://www.hippocrates-imi.eu/about/funding>. EFPIA: European Federation of Pharmaceutical Industries and Associations; HIPPOCRATES: Health Initiatives in Psoriasis and Psoriatic Arthritis Consortium European States; JU: Joint Undertaking.

Table. The GRAPPA project team for the slide library update.

Section	Senior Advisor: Rheumatologist	Senior Advisor: Dermatologist	Y-GRAPPIAns
Genetics	Proton Rahman	Mona Stahle	Sebastián Herrera
Pathogenesis and tissues	Christopher Ritchlin, Kurt de Vlam	Luis Puig	Hanna Johnsson
Classification, epidemiology, and prognosis	Philip Helliwell, Vinod Chandran	Laura Savage	Pamela Diaz, Francesco Bellinato
Clinical features	Dafna Gladman	Amit Garg	Anand Kumthekar
Imaging	Lih Eder, Denis Poddubnyy	NA	Cristina Macia, Ummugulsum Gazel
PsO treatment	NA	Laura Ferris, Joseph F. Merola	Betul Macit, Guilherme Muzy
PsA treatment	Arthur Kavanaugh, Philip Mease	NA	André Ribeiro, Olafur Pálsson
Outcome measures	Laura Coates	Kristina Callis Duffin	Tania Gudu
Skin	NA	Wolf-Henning Boehncke	Giovanni Damiani
Nails	NA	Kristina Callis Duffin	Dimitri Luz
Comorbidities	M. Elaine Husni, Deepak Jadon	Paolo Gisondi, Jason Hawkes	Estella Chen, Silvia Scriffignano, Barbara Hernandez Agustina

GRAPPA: Group for Research and Assessment in Psoriasis and Psoriatic Arthritis; NA: not applicable; PsO: psoriasis; PsA: psoriatic arthritis; Y-GRAPPIAns: Young-GRAPPA members.

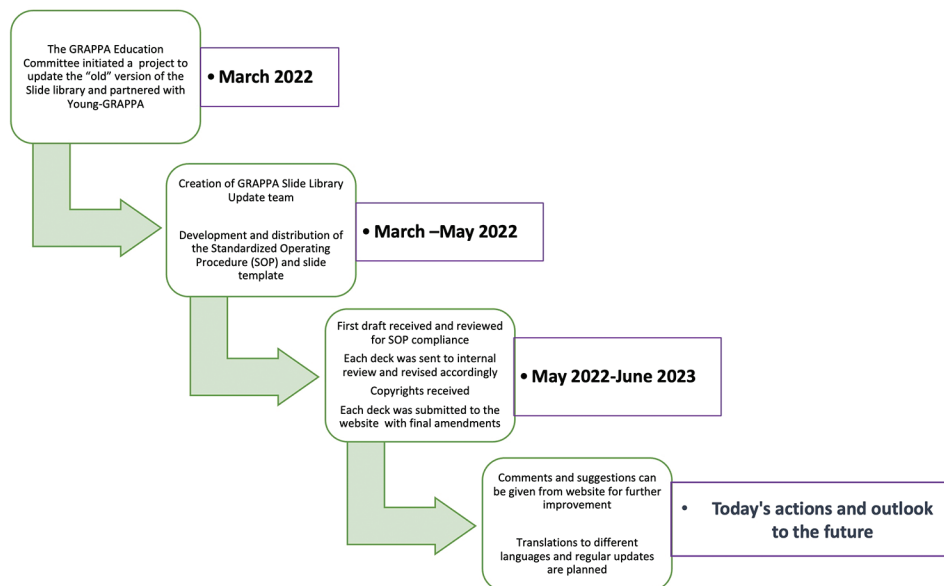


Figure 3. Key steps and timelines for the development of the GRAPPA slide library. GRAPPA: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; SOP: standard operating procedure.

The comprehensive process was finalized in June 2023. The GRAPPA slide library was launched in July 2023, with the unveiling of an invaluable resource at the annual trainee symposium, and can be found here: <https://slides.grappanetwork.org>. The slide library will continue to evolve and improve with regular updates and new steps, including translations to different languages to reach a larger audience.

Treatment recommendations update, by Drs. Laura Coates, Arthur Kavanaugh, and Enrique Soriano

During the annual meeting in 2023, the GRAPPA treatment recommendations committee presented a summary on the progress made with the 2022 publication as well as a proposed timeline for future updates. The 2022 treatment recommendations and the supporting literature reviews are all now published.³⁻¹¹

The recommendations have been well received and widely disseminated through educational talks and other presentations. In conjunction with *Nature Reviews Rheumatology*, they have also now been translated into Spanish and Portuguese and are available for download from the journal's website: https://static-content.springer.com/esm/art%3A10.1038%2Fs41584-022-00798-0/MediaObjects/41584_2022_798_MOESM1_ESM.pdf.

Ongoing development of the current treatment recommendations remains part of the core mission of GRAPPA. Progress in the field will necessitate another new update in the not-too-distant future. The process of developing the 2022 recommendations took over 2 years, with delays introduced by the global coronavirus disease 2019 pandemic. Therefore, it is important to plan for the next update and start on the literature review process again. As part of the initiation of the process, volunteers for each domain were requested from the GRAPPA membership. Similar to the current version, support for the methodology of the systematic literature review will be outsourced. This will provide additional support for GRAPPA members working on the project and will ensure high-quality review prior to submission. We plan to start this process in 2024 and will share further details with the GRAPPA membership then.

Conclusion

This paper outlines some of GRAPPA's recent major research and educational activities that were presented during the 2023 annual meeting. These initiatives align with GRAPPA's mission of addressing educational and research needs in PsD, fostering community networking, and enhancing patient care through collaborative networks and treatment recommendations.

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