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GRAPPA 2023 Collaborative Research Network Meeting

Vinod Chandran[1], Dafna D. Gladman[2], Philip J. Mease[3], Lihi Eder[4], Stephen R. Pennington[5], Oliver FitzGerald[5], Christopher Ritchlin[6], Dan E. Webster[7], Kurt de Vlam[8], and Wilson Liao[9]

ABSTRACT. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Collaborative Research Network (CRN)/research committee met during the GRAPPA 2023 annual meeting. Updates were provided on GRAPPA research projects, including the Axial Involvement in Psoriatic Arthritis (AXIS), Axial Psoriatic Arthritis Molecular and Clinical Characterisation Study, Diagnostic Ultrasound Enthesitis Tool (DUET), and Sex- and Gender-Based Analysis of the Effectiveness of Advanced Therapies (SAGE) studies, as well as the Health Initiatives in Psoriasis and Psoriatic Arthritis Consortium European States (HIPPOCRATES) and Elucidating the Landscape of Immunoendotypes in Psoriatic Skin and Synovium (ELLIPSS) studies. The highlight of the meeting was a presentation and discussion on the use of digital tools to study psoriatic disease.

Key Indexing Terms: biomarkers, GRAPPA, psoriasis, psoriatic arthritis, spondyloarthritis

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Collaborative Research Network (CRN) held its annual meeting during the GRAPPA 2023 annual meeting in Dublin, Ireland. Prof. Wilson Liao welcomed attendees and discussed the mission of the CRN, which is to facilitate global collaborative psoriatic disease (PsD) research by fostering collaboration and cooperation between stakeholders worldwide. The activities of the GRAPPA CRN/research committee were reviewed. The committee comprises 3 cochairs and 15 members, which include patient research partners and Young-GRAPPiAns. Each member's term is 3 years with 1 renewal. Liao mentioned that collaborative research projects could be initiated by GRAPPA member(s) (funded by single or multiple industry partners or other funding agencies) or by industry partners. The GRAPPA research committee encourages GRAPPA members to propose research projects to address unmet needs in PsD. On receipt of a proposal, the committee reviews the merits of the proposal and, if found meritorious, work with the proposers to obtain funding and execute the project. There was interest among the members of the research

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[1]V. Chandran, MBBS, MD, DM, PhD, Division of Rheumatology, Departments of Medicine and Laboratory Medicine and Pathobiology, University of Toronto, and Krembil Research Institute, University Health Network, Toronto, Ontario, Canada; [2]D.D. Gladman, MD, Division of Rheumatology, Department of Medicine, University of Toronto, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto, Ontario, Canada; [3]P.J. Mease, MD, Swedish Medical Center/Providence St. Joseph Health, and University of Washington School of Medicine, Seattle, Washington, USA; [4]L. Eder, MD, PhD, Women's College Research Institute, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; [5]S.R. Pennington, PhD, O. FitzGerald, MD, School of Medicine, UCD Conway Institute for Biomolecular Research, University College Dublin, Dublin, Ireland; [6]C. Ritchlin, MD, MPH, Professor of Medicine, Allergy, Immunology, and Rheumatology Division, Center for Musculoskeletal Research, University of Rochester Medical School, Rochester, New York, USA; [7]D.E. Webster, PhD, AbbVie Inc., North Chicago, Illinois, USA; [8]K. de Vlam, MD, PhD, Department of Rheumatology, University Hospitals Leuven, and Skeletal Biology and Engineering Research Center (SBE), Dept Development and Regeneration, KU Leuven, Leuven, Belgium; [9]W. Liao, MD, Department of Dermatology, University of California San Francisco, San Francisco, California, USA.

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Address correspondence to Dr. K. de Vlam, Department of Rheumatology, University Hospitals Leuven, Skeletal Biology and Engineering Research Center (SBE), Dept Development and Regeneration, KU Leuven, Herestraat, 49-B3000 Leuven, Belgium. Email: Kurt.devlam@uzleuven.be.

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committee in fostering special interest groups for research in focused areas such as synovitis, pustular psoriasis (PsO), and imaging, to name a few. The research committee is also interested in developing equitable short-term trainee/junior faculty mentorship programs, including grant-writing workshops. Additionally, the research committee administers the GRAPPA pilot research grant program. The criteria for judging these grants include innovation, relevance to PsD, feasibility, budget, and approach.

Prof. Kurt de Vlam led the discussion on current projects. Prof. Dafna Gladman reviewed the status of the Axial Involvement in Psoriatic Arthritis Cohort (AXIS) study.[1] This international study, which includes 57 centers in 21 countries, aims to determine the frequency of axial involvement in psoriatic arthritis (PsA). Of the proposed target of 400 patients, 294 had been recruited by the time of the GRAPPA 2023 meeting. Prof. Philip Mease reviewed the progress of the Axial PsA Molecular and Clinical Characterisation Study. This multicenter study aims to identify liquid and tissue markers that differ between patients with PsA with axial disease from those without axial disease, primarily defined by imaging. The aim is to recruit 20 patients with axial disease and 20 patients without axial involvement who are naïve to targeted therapies and who have a disease duration < 10 years. In addition to clinical and imaging information, blood and stool samples will be collected in all patients, and synovial biopsies and skin biopsies in at least 50% and 80% of patients, respectively. Of the 9 sites participating, 1 has recruited 5 subjects. Contracts are being finalized at all other sites.

Dr. Lihi Eder reviewed 2 studies that she is leading. The Diagnostic Ultrasound Enthesitis Tool (DUET) study aims to develop a diagnostic sonographic score for enthesitis that discriminates PsA from non-PsA. This cross-sectional study in 17 sites in 8 countries recruited 215 subjects with PsA within 5 years of diagnosis, 100 subjects with PsO and no musculoskeletal symptoms, and 106 controls with noninflammatory rheumatic conditions such as osteoarthritis and fibromyalgia. Study procedures included physical exam, patient surveys, and ultrasound scanning of 16 entheseal sites. The scans were read by 2 central readers and a local reader. Analyses are ongoing to determine informative entheseal lesions and sites, effect of contextual factors such as BMI, and the score's discriminative ability. The second study, titled Sex- and Gender-Based Analysis of the Effectiveness of Advanced Therapies (SAGE), aims to understand the influence of sex and gender on response to treatment with targeted therapies in PsA. Since the last update, the study has secured funding for clinical aspects. Thirty-six sites worldwide have been recruited and the first patient was enrolled in March 2023. Translations of the questionnaires to 12 languages have been completed.

Profs. Stephen Pennington and Oliver FitzGerald provided an update on the status of the Health Initiatives in Psoriasis and Psoriatic Arthritis Consortium European States (HIPPOCRATES) study (https://www.hippocrates-imi.eu/). This study now has 27 partners in 11 countries, with strong engagement from 5 pharmaceutical company partners. The study has 8 work packages. The study focuses on predicting PsA in people with cutaneous PsO, early diagnosis, damage progression, and predicting treatment response. Consortium-wide material transfer and data sharing agreements have been finalized. The Swiss Institute of Bioinformatics will securely host the study's data management platform. An important substudy is the HIPPOCRATES Prospective Observational Study (HPOS), led by Profs. Laura Coates, Pennington, and FitzGerald, which will recruit 25,000 subjects with cutaneous PsO across Europe to an online study with the aim of identifying patients with high risk of developing PsA (https://www.hpos.study). Consent will be obtained remotely. The website has been developed and translated to multiple languages. The intention is also to collect biosamples (blood from a finger prick) remotely from 3000 selected participants for biomarker analyses.

Prof. Christopher Ritchlin described the National Institutes of Health Accelerating Medicines Partnership (NIH-AMP)–supported Elucidating the Landscape of Immunoendotypes in Psoriatic Skin and Synovium (ELLIPSS) study. This study aims to study the histopathology and key cell subsets in PsO and PsA in comparison to systemic lupus erythematosus and rheumatoid arthritis using single-cell RNA sequencing and spatial transcriptomics, among other techniques. The ELLIPSS study aims to tie endotypes, including the role of B cells, to various phenotypes including comorbidities, treatment response, and transition from PsO alone to PsA. The role of bile acids in psoriatic inflammation will also be explored by studying the gut and skin microbiome along with the metabolome. Further, uveitis is an important associated disease in patients with PsO and PsA. An important substudy is to investigate uveitis in PsD using tear proteomics, microbiomics, and single-cell RNA sequencing of vitreous fluid.

To wrap up this CRN meeting, Dr. Dan Webster discussed digital tools to measure PsD. Webster focused on using smartphone-based measurements to capture signs and symptoms of PsD. High-quality imaging from smartphone cameras can capture skin and nail manifestations, whereas smartphone motion sensors can assess functional movement impairment resulting from musculoskeletal symptoms. These sensor-based measurements can be performed by patients at home to provide more continuous assessment of PsD between periodic clinical visits.

Webster discussed the formation of the Psorcast Digital Biomarker Consortium to create and validate a suite of smartphone-based assessments for PsD.[2] The consortium was the product of academic/nonprofit and industry collaboration between Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network Consortium (PPACMAN), Sage Bionetworks, Novartis, UCB, Janssen, and Pfizer that brought together clinical, scientific, and technology development partners.[3] The principal use case for this technology was investigating the transition from PsO to PsA, in which early detection and intervention may prevent disease progression. The key achievements of the Psorcast Digital Biomarker Consortium to date have been the development of the Psorcast iOS application,[4] a cross-sectional clinical validation study demonstrating the accuracy of the measurements in patients with PsO and PsA, and a decentralized research study in which patients throughout the United States can consent, enroll, and self-measure their symp-

toms over time while contributing relevant patient-reported history and contextual information about their disease management and outcomes (www.psorcast.org).[5]

The discussion of the Psorcast app included a compelling case study of Psorcast's innovative approach using smartphone photography for assessing signs of joint swelling, nail PsO, and dactylitis. Patients can photograph each hand using the app and these images are then analyzed at the level of each digit relative to its contralateral counterpart as a control to assess for dactylitis. This approach has the potential to provide a similar measurement to the Leeds dactylometer in a fraction of the time and allow for regular self-monitoring by patients outside of a clinical setting.[6]

The patient-generated images of each hand are also assessed for nail PsO using machine learning/artificial intelligence (AI). The Psorcast team trained a deep learning classification model to detect nail PsO with an accuracy of 76%, performing comparably to a panel of remote physician raters.[5] Notably, the model maintains its accuracy even in scenarios where physicians report uncertainty in their diagnosis, underscoring the robustness of AI-assisted tools in assisting clinicians in managing complex diseases like PsD.

The last point discussed in this case study using patient-captured hand images was the ability to estimate a patient's Fitzpatrick skin type. This allowed the team to report on the relative contributions of each skin tone to the classification model's training set. The validation study cohort comprised Fitzpatrick skin types 1 to 5. A categorical comparison between each skin type showed equivalent accuracy for classification, demonstrating the generalizability of the tool and model. Webster described the crucial role that digital measurement tools play in assessing and improving the generalizability of machine learning and AI models. Often, these models are trained on nonrepresentative cohorts, leading to limitations in their real-world applicability. By incorporating data from a broader, more diverse patient population through digital tools, the accuracy and utility of these models can be significantly enhanced.

Webster concluded his presentation by noting that the current landscape of digital tools for PsD is diverse, yet incomplete. He described 3 categories of digital measurement tools: (1) patient/clinical education tools, (2) remote patient monitoring tools, and (3) drug development tools. Whereas patient and clinical education tools and remote patient monitoring tools (including Psorcast) have seen significant development, the area of digital drug development tools remains largely unexplored. Dr. Webster pointed to the complete absence of these tools for PsD in the US Food and Drug Administration (FDA)'s drug development tool qualification program.[7] This gap presents a unique opportunity for GRAPPA and for academic and industry collaboration to foster innovation in this space. Digital drug development tools provide similar functionality to remote patient monitoring tools but have the added validity of having attained the requisite regulatory approval and evidentiary requirements and validation for use in clinical trials. Regulators have signaled their readiness for these types of submissions; notably, the FDA formed the Digital Health Center of Excellence and recently released guidance entitled, "Digital health technologies for remote data acquisition in clinical investigations."[8] The regulatory acceptance of these digital tools and adoption in clinical research would provide unprecedented insight into the time-series dynamics of drug response, onset and relief of flares, and long-term monitoring of disease progression.

Perhaps the most impactful point discussed related to digital measurement tools was the potential for a groundbreaking shift in the role of the patient in research and care. Digital measurement tools allow patients to take an active role in objectively measuring their own disease at the points when it is affecting their lives the most. These moments can then be considered by clinical care teams during decision making. The collaboration between academia and industry will be pivotal in realizing this potential, paving the way for a new era in clinical research, effective disease management, and access to care.

To conclude, the CRN meeting provided an update of the current activities of the GRAPPA CRN/research committee to the larger membership. Significant progress made in multiple studies was acknowledged and the results of the studies are highly anticipated. Using digital tools to understand dynamic changes in PsD status has the potential to revolutionize patient care.

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