GRAPPA 2017 Project Report

Kristina Callis Duffin, Oliver FitzGerald, Artie Kavanaugh, Philip J. Mease, Joseph F. Merola, Alexis Ogdie, Denis O'Sullivan, Soumya M. Reddy, Christopher T. Ritchlin, and Laura C. Coates

ABSTRACT. At the 2017 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), members received updates on several ongoing educational and research efforts. Among them were updates on GRAPPA's continued education efforts; GRAPPA's continued research efforts, including the Biomarker Project, a collaborative research effort to identify and study biomarkers of joint damage; treatment recommendations, including recommendations and core principles related to biosimilars; efforts to update GRAPPA's Website and to create a GRAPPA smartphone application (app); and the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network. (J Rheumatol Suppl. 2018 June;94:48–51; doi:10.3899/jrheum.180139)

Key Indexing Terms:
PSORIASIS PSORIATIC ARTHRITIS EDUCATION RESEARCH GRAPPA PPACMAN

Members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) continue to pursue core objectives of GRAPPA's mission, specifically providing education, identifying research assessment tools, and pursuing research in disease pathophysiology. At the 2017 annual GRAPPA meeting, members received updates on GRAPPA's continued education efforts; GRAPPA's continued research efforts, including the Biomarker Project, a collaborative research effort to identify and study biomarkers of joint damage; treatment recommendations, including recommendations and core principles related to biosimilars; efforts to update GRAPPA's Website and to create a GRAPPA smartphone application (app); and the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (PPACMAN).

From the University of Utah, Salt Lake City, Utah; University of California at San Diego, La Jolla, California; Rheumatology Research, Swedish Medical Center and University of Washington School of Medicine, Seattle, Washington; Department of Dermatology and Medicine, Division of Rheumatology, Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts; Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; New York University School of Medicine, New York; Division of Allergy, Immunology, and Rheumatology, University of Rochester Medical Center, Rochester, New York, USA; Newman Clinical Research Professor, Department of Rheumatology, St. Vincent's University Hospital; Conway Institute for Biomolecular Research, University College Dublin; Our Lady's Hospice and Care Services, Dublin, Ireland; Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, University of Oxford, Oxford, UK.

As part of the supplement series GRAPPA 2017, this report was reviewed internally and approved by the Guest Editors for integrity, accuracy, and consistency with scientific and ethical standards.

K. Callis Duffin, MD, University of Utah; O. FitzGerald, MD, FRCPI, FRCP(UK), Newman Clinical Research Professor, Department of Rheumatology, St. Vincent's University Hospital, and Conway Institute for Biomolecular Research, University College Dublin; A. Kavanaugh, MD, Professor of Medicine, University of California at San Diego; P.J. Mease, MD, Rheumatology Research, Swedish Medical Center and University of Washington School of Medicine; J.F. Merola, Department of Dermatology and Medicine, Division of Rheumatology, Harvard Medical School, Brigham and Women's Hospital; A. Ogdie, MD, Assistant Professor of Medicine and Epidemiology, Perelman School of Medicine, University of Pennsylvania; D. O'Sullivan, BE, Patient Research Partner, Our Lady's Hospice and Care Services; S. Reddy, MD, Assistant Professor of Medicine, New York University School of Medicine; C.T. Ritchlin, MD, MPH, Professor of Medicine, Division of Allergy, Immunology, and Rheumatology, University of Rochester Medical Center; L.C. Coates, MBChB, PhD, Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, University of Oxford.

Address correspondence to L.C. Coates, Botnar Research Centre, Windmill Road, Oxford, 0X37LD, UK. E-mail: laura.coates@ndorms.ox.ac.uk

Educational Committee

A core objective of GRAPPA's mission is education. GRAPPA members around the world provide psoriasis and psoriatic arthritis (PsA) education to many people, including other healthcare professionals (physicians, nurses, physician assistants, medical students, residents, and fellows), patients and their families, and those otherwise involved in the care of patients with psoriasis and PsA (people working in healthcare agencies, payor groups, and pharmaceutical company employees). This education is provided in many forms, including live lectures, hands-on patient workshops, Webcasts and audioconferences, online reading material and slides, articles for publication in medical journals, textbook chapters, and brochures for patient-service leagues.

Because of GRAPPA's global reach, education occurs in many languages, sometimes aided by simultaneous translators, and with appropriate cultural sensitivity. Although much of this activity is conducted by GRAPPA alone, GRAPPA performs many of these efforts in collaboration with other organizations such as the National Psoriasis Foundation (NPF), the International Federation of Psoriasis Associations, the Arthritis Foundation, the American College of Rheumatology (ACR), the European League Against Rheumatism (EULAR), the Pan American League Against Rheumatism, the Asian Pacific League Against Rheumatism, the Assessment of Spondyloarthritis international Society (ASAS), and the Spondyloarthritis Assessment and Treatment Network (SPARTAN).

In 2016 and 2017, an ongoing collaboration between GRAPPA and SPARTAN yielded a number of half- and full-day continuing medical education symposia on PsA, psoriasis, and spondyloarthritis in New York, Cleveland, New Orleans, Dallas, Boston, Denver, and Salt Lake City. In addition, GRAPPA has continued to collaborate with ASAS to conduct a well-attended symposium at the ACR meeting, which took place in Washington, D.C., in 2016 and San Diego in 2017. In each of these settings, junior and regionally derived faculty teach alongside senior GRAPPA faculty members. These symposia are supported by unrestricted educational grants from pharmaceutical sponsors, including Abbvie, Janssen, Celgene, Amgen, and Mallinckrodt. European symposia have been conducted in cities such as Leeds, London, Milan, Stockholm, Paris, Rome, and Utrecht. Symposia have also been conducted in other countries, including Japan, Korea, China, and Brazil, with sponsorship that has included Abbvie, Janssen, and UCB.

To aid with lectures, GRAPPA has developed an educational slide library for speakers to use that is updated as new information about disease or treatment emerges. In addition, GRAPPA members have developed online videos that teach students, residents, fellows, and clinical trial investigators how to properly examine skin, nails, joints, spine, and entheses.

Plans for future GRAPPA educational activities include updating GRAPPA's physical examination Web-based teaching modules, developing additional online education modules, developing GRAPPA smartphone apps, educating dermatology residents and rheumatology fellows on psoriasis and PsA as part of their training in academic centers, and continuing to educate healthcare providers and patients about PsA in underresourced parts of the world. The GRAPPA education committee is co-chaired by Philip J. Mease, MD (Seattle, Washington, USA), and Amit Garg, MD (Lake Success, New York, USA).

Biomarker Project

At the GRAPPA 2017 annual meeting in Amsterdam, the Netherlands, Dr. Oliver FitzGerald (Dublin, Ireland) provided an update on the proposed PsA Biomarkers of Damage project and reported that significant progress has been made in negotiations with industry partners. Amgen, which is conducting the Study of Etanercept and Methotrexate in Combination or as Monotherapy in Subjects with Psoriatic Arthritis (SEAM) study (NCT02376790), has been collecting appropriate imaging and bio-samples and has agreed in principle to share these samples with GRAPPA. A contract between Amgen and GRAPPA is under negotiation and should be finalized in the near future. Because it will be important to be able to validate any biomarker findings in independent cohorts, discussions are also under way with both Pfizer and Lilly. These discussions include but are not limited to the tofacitinib and ixekizumab studies, respectively, but also determining biomarkers of treatment response and biomarkers of disease activity.

Dr. FitzGerald highlighted 3 recent studies that demonstrate continued progress in biomarker development. The first study demonstrated how baseline levels of serum CXCL10 (which recruits inflammatory cells to sites of inflammation) have been shown to be increased in patients with psoriasis who converted to PsA as compared to those who did not convert[1]. Interestingly, levels appear to fall again following conversion to PsA. While validation is required, these data suggest that CXCL10 levels may be useful as a way to monitor patients with psoriasis for the development of PsA. The second study identified a panel of serum proteins that clearly separates early PsA from rheumatoid arthritis (RA) with an area under the curve (AUC) of 0.9 (unpublished). Validation work is ongoing with biomarker panel testing by Multiple Reaction Monitoring being undertaken in a number of disease cohorts. The third study, conducted by Siebert, *et al*[2], reported on panels of urine peptides that were each specific for disease cohorts that included PsA, RA, osteoarthritis, inflammatory bowel disease (as an inflammatory control group), and normal controls. The AUC were all > 0.9 when comparing each individual disease with the other groupings combined. These results suggest that multibiomarker panels may offer promise as diagnostic tests for rheumatic diseases including PsA.

Research Committee

The Research Committee, under the leadership of Drs. Christopher T. Ritchlin (Rochester, New York, USA) and April W. Armstrong (Los Angeles, California, USA), released a request for applications from trainees and junior investigators for pilot projects in psoriasis and PsA. In 2017, GRAPPA received 23 applications and funded 5 proposals at $25,000 each. These proposals were awarded to: (1) C. Magee (Ireland), Biomarkers of progression to PsA; (2) L. Eder (Canada), Psoriasis to PsA transition; (3) M. van Mechelen (Belgium), Role of biomechanical stress and psoriasis in PsA; (4) J. Manasson (USA), Effect of biologics on gut microbiome and PsA; and (5) H.J. Weng (Taiwan), Neural pruritus mechanisms in psoriasis. The Research Committee sent a new request for applications in February 2018 with additional information and details provided at that time.

After considerable discussion within the steering committee and relevant committees involved, it was decided to merge the Biomarkers and Research Committees. The biomarker efforts have greatly expanded and dovetail well with the Research Committee's activities. Drs. FitzGerald, Ritchlin, and Armstrong will co-chair the committee and will oversee the development of the GRAPPA Collaborative Research Network and Biorepository. This work is well under way[3].

Additional changes to the Research Committee were also discussed and agreed upon. GRAPPA will establish both a Trainees Symposium Sub-Committee to help plan, organize,

and supervise the Trainees Symposium, as well as a Research Grant Review Committee to oversee GRAPPA's grant evaluation program. Several GRAPPA members have expressed interest in joining these committees, and members were formally invited to join by January 2018.

Treatment Recommendations Update

The ACR and NPF are collaborating to develop treatment guidelines for the management of PsA. The guideline development process differs from that used by GRAPPA and EULAR in the use of the Grades of Recommendation, Assessment, Development, and Evaluation methodology. The process began in September 2016 with a meeting held to determine the scope of the guidelines. The draft treatment guideline was presented at the ACR meeting in November 2017 in San Diego, California, USA.

When the 2015 GRAPPA treatment recommendations update was published[4], it was clear that the brisk pace of relevant developments in therapies for psoriasis and PsA would make it necessary to provide periodic treatment recommendation updates covering key emerging topics prior to the next complete revision. Biosimilars, now in broad use across the globe, were one of the initial key topics[5]. A multidisciplinary, international group of GRAPPA members, including patient research partners, discussed the topic. The group agreed upon the following core principles:

1. Biosimilars must be approved through a robust regulatory review; "biomimics" or "intended copies" are not biosimilars, which should be clearly understood.
2. Periodic reevaluation of biosimilar products post-approval is important to ensure ongoing quality.
3. Extrapolation to psoriasis or PsA, even when no studies are conducted in psoriasis or PsA, is acceptable; ideally, additional studies specifically in psoriasis and PsA should be conducted after approval.
4. Patients and physicians need to be involved in decisions about switching therapies.
5. Pharmacovigilance is crucial, and naming conventions need to allow for the tracking of specific agents and batches.
6. Multiple switches of biosimilars should be studied in a rigorous fashion.
7. Savings realized from the use of biosimilars should be utilized to improve access to these biologic agents for a larger number of patients.
8. Immunogenicity is a concern that should be monitored on an ongoing basis.

In addition to the recommendations developed by consensus, a research agenda will address additional relevant issues in the publication and recommend future research.

Website and Smartphone App Development

In 2015, the GRAPPA Website underwent renovation and rebranding and was relaunched in 2016. In September 2016, GRAPPA successfully bid its first competitive funding program with the Independent Grant for Learning and Change program run by Pfizer. The funding was used to establish an online learning portal that addresses recently published GRAPPA Treatment Recommendations. The grant was submitted as a collaboration between a committee of GRAPPA members and Guideline Central. GRAPPA had previously partnered with Guideline Central to design and produce a quick reference guide about GRAPPA treatment recommendations. The technical expertise that GRAPPA's prior partnership with Guideline Central provided aided in the development of this online GRAPPA Treatment Recommendation learning portal.

The online portal went live on September 1, 2017, and is available to all, regardless of GRAPPA membership. All GRAPPA members were sent a link on launch, and the Website is available from the GRAPPA educational page. The portal includes 4 modules that discuss overarching treatment principles, optimal treatment choices, new therapies, and comorbidities in PsA. Each module has a slide presentation with an audio narration covering key points from treatment recommendations and beyond. Participants can complete pre- and post-presentations test questions to test their knowledge and can compare their scores with other participants. Interactive case studies are also included that illustrate the material discussed in each module.

In 2017, GRAPPA began to develop a smartphone app to aid physicians in clinical practice. The app will include information on GRAPPA and PsA; a module to calculate the Psoriasis Area and Severity Index and body surface area; a module that allows patients to complete the PsA Impact of Disease (PsAID) questionnaire and that calculates and presents its results to the physician and patient; and a module to assess treat-to-target goals in PsA that calculates very low disease activity and minimal disease activity. The app will not record any data internally to avoid any data protection issues. It will be free to download and available in both Android and Apple formats.

Initially, the PsAID questionnaire module will be available in 11 languages: English, French, German, Spanish, Portuguese, Italian, Arabic, traditional Chinese, simple Chinese, Japanese, and Russian. If demand exists, additional languages could be added in future versions. GRAPPA will track the number of downloads of the app by country. This information will help to prioritize which new languages should be added in possible future versions of the PsAID module.

The app is now available in English, and additional languages will become available through 2018. It will be promoted through GRAPPA educational activities to ensure that physicians worldwide are aware of this resource.

The Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (PPACMAN)

Dermatologists and rheumatologists each play a key role in

the management of PsA. Diagnosis and treatment decisions for the patient with psoriatic disease can be complex. The relative severity of skin and musculoskeletal manifestations, as well as a host of potential drug interactions and potential comorbid, co-prevalent conditions, further complicate PsA treatment decision making.

Combined clinic models present a unique multidisciplinary care delivery model for patients with psoriatic disease. Patients benefit from these models through increased education and support for the many aspects of their disease, a "one-stop shopping" model, access to a wider array of therapies, combined discussions with their dermatologist and rheumatologist, and a quicker transition to appropriate systemic therapy, including disease-modifying antirheumatic drugs and biologics. Clinicians benefit from these models through increased collegiality, cross-disciplinary education, and increased work satisfaction. Rheumatology trainees benefit from these models through their increased awareness of the differential diagnosis of presenting skin disorders and comfort in the use of topical agents; dermatology trainees benefit from an increased awareness of the rheumatology evaluation and examination. These elements were previously reported in the *PPACMAN Survey of Benefits and Challenges to Combined Rheumatology-Dermatology Clinics* publication in 2017[6].

PPACMAN is a nonprofit corporation whose mission is to encourage psoriatic disease combined clinics and centers in both academic and community settings. The combined sites are meant to advance a multilevel approach for psoriatic patients, increase disease awareness, and accelerate disease management. PPACMAN does this through educational, administrative, and research activities. It seeks to improve education about the importance of PsA screening, the early identification of PsA, and the value of collaborative care for patients with psoriatic disease. It also supports the formation of combined multidisciplinary clinic models and regional dermatologist-rheumatologist partnerships. PPACMAN provides opportunities for trainees and practicing dermatologists and rheumatologists to travel to sites within the North American network to observe a combined clinic model. PPACMAN is also developing a core curriculum in the management and collaborative care of psoriatic patients.

PPACMAN's research goals include the evaluation of multisite PsA screening processes, multidisciplinary shared note templates for data collection across network sites, the effectiveness of these novel care delivery models (i.e., defining ideal care outcomes), and comorbidity identification. In the future, PPACMAN would like to offer small pilot grants to investigators who are actively developing lines of research that address collaborative care models in psoriatic diseases.

This paper summarizes GRAPPA's recent work on a number of projects. These projects are part of GRAPPA's core roles: to address educational and unmet research needs, to create opportunities for networking within the psoriatic community, and to optimize patient care through collaborative care networks and treatment recommendations. These projects are ongoing and should continue to add value in the years to come.

REFERENCES

1. Abji F, Pollock RA, Liang K, Chandran V, Gladman DD. Brief report: CXCL10 is a possible biomarker for the development of psoriatic arthritis among patients with psoriasis. Arthritis Rheumatol 2016;68:2911-6.
2. Siebert S, Porter D, Paterson C, Hampson R, Gaya D, Latosinska A, et al. Urinary proteomics can define distinct diagnostic inflammatory arthritis subgroups. Sci Rep 2017;7:40473.
3. Jadon DR, Chandran V, Stober C, Ogdie A, Armstrong AW, Duffin KC, et al. Proceedings of the 2017 GRAPPA Collaborative Research Network (CRN) meeting. J Rheumatol Suppl. 2018 June; 94:54-61.
4. Coates LC, Kavanaugh A, Mease PJ, Soriano ER, Laura Acosta-Felquer M, Armstrong AW, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis. Arthritis Rheumatol 2016;68:1060-71.
5. Kay J, Schoels MM, Dorner T, Emery P, Kvien TK, Smolen JS, et al; Task Force on the Use of Biosimilars to Treat Rheumatological Diseases. Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases. Ann Rheum Dis 2018;77:165-74.
6. Okhovat JP, Ogdie A, Reddy SM, Rosen CF, Scher JU, Merola JF. Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network Consortium (PPACMAN) survey: benefits and challenges of combined rheumatology-dermatology clinics. J Rheumatol 2017;44:693-4.