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2021 GRAPPA Meet the Experts Session: A Summary of Presentations

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ABSTRACT. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis hosted a Meet the Experts session at its 2021 virtual meeting. Dermatology and rheumatology experts held 5 sessions that broadly centered on psoriasis and psoriatic arthritis.

Key Index Terms: GRAPPA, psoriasis, psoriatic arthritis

Introduction

At the 2021 Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) annual meeting, 5 Meet the Experts sessions were held. These sessions allowed rheumatology and dermatology experts to share new research and clinical findings on psoriatic disease (PsD) with the larger psoriasis (PsO) and PsD specialist community. The incoming GRAPPA copresidents, Prof. Oliver FitzGerald and Dr. April Armstrong, facilitated the 5 sessions and moderated the question-and-answer portion, where presenters addressed questions from the audience. The following are brief summaries of the 5 Meet the Experts sessions.

1. Session With Dr. April Armstrong and Prof. Oliver Fitzgerald

In this Meet the Experts session, the future of GRAPPA was discussed including the benefits of a GRAPPA copresidency and ideas to encourage more involvement by dermatologists. In addition, the most up-to-date treatment recommendations for PsD were covered.

As the GRAPPA organization continues to grow, the responsibilities of the presidency have increased substantially. GRAPPA leadership decided that the best way to promote the goals of the organization was to develop a leadership structure that allowed representation of both rheumatology and dermatology specialties. It was agreed to move forward with a GRAPPA copresidency, with one copresident being a dermatologist (Dr. Armstrong) and the other a rheumatologist (Prof. FitzGerald). The benefits of a shared copresidency were discussed, such as promoting greater dermatologist participation in the organization and a more streamlined emphasis on both rheumatology and dermatology collaborative research.

As part of the supplement series GRAPPA 2021, this report was reviewed internally and approved by the Guest Editors for integrity, accuracy, and consistency with scientific and ethical standards.

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Planning for how to move GRAPPA forward in 2021–2024, the copresidents proposed initiatives aiming to encourage representation and long-term participation of younger GRAPPA members, especially younger dermatologists. To accomplish this goal, the copresidents will support the development of a "Young GRAPPA" group. Additional ideas included continuing future GRAPPA leadership retreats, perhaps the day before the 2022 annual meeting. The GRAPPA retreat would address the evolution and future of GRAPPA, cultivate initiatives such as the patient education committee, and highlight scientific writing and collaborative research.

Next, the 2021 update of the GRAPPA treatment recommendations was reviewed. Prof. FitzGerald highlighted the overarching therapeutic principle of consideration of all disease domains in the assessment and treatment of PsD. The treatment recommendations encourage the inclusion of patient-reported outcome measures (PROMs) and the evaluation of comorbidities and related conditions in clinical assessments of PsD. In addition, they promote multidisciplinary and multispecialty care for people with PsO, with an emphasis on individualized therapeutic decisions made jointly between patient and physician.

For the treatment of plaque PsO, GRAPPA strongly recommends topical therapies, phototherapy, and conventional systemic therapies, with a conditional recommendation for acitretin. For the treatment of nail PsO, GRAPPA strongly recommends systemic therapies, specifically all 4 classes of biologics, given that nail PsO has been shown to be resistant to topical therapies. The European Alliance of Associations for Rheumatology 2019 algorithm for treatment of psoriatic arthritis (PsA) encourages early dermatology consultation for cases of major skin involvement. Major changes in the American Academy of Dermatology National Psoriasis Foundation treatment guidelines for plaque PsO were discussed. The updated guidelines suggest that yearly tuberculosis (TB) tests should be conducted only in high-risk populations, such as those in contact with persons who have active TB or are on tumor necrosis factor inhibitors (TNFi). In addition, dose escalation of biologics should initially be accomplished by shortening dosage intervals prior to increasing dosages.

Last, specific treatment recommendations for individuals with PsA who are disease-modifying antirheumatic drug (DMARD)-naïve or have failed initial biologic therapy were addressed. For DMARD-naïve patients, the recommendations suggest conventional systemic DMARDs including biologics. For those who failed initial biologic therapy, the main recommendation is to consider alternate biologics. The session concluded by addressing any questions or concerns from the audience.

2. Session With Dr. Kristina Callis Duffin and Dr. Philip Helliwell

This session provided a description of SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteomyelitis) syndrome, followed by discussion of patient cases.

SAPHO syndrome is rarely seen in rheumatological and dermatological practices. The syndrome was first described by Chamot et al in France but has a higher prevalence in Japan.[1] Most individuals present initially with rheumatologic manifestations, primarily anterior chest wall pain due to osteitis of the bones of the anterior chest and inner third of the clavicle or synovitis of the sternoclavicular and manubriosternal joints.[2] Others may have peripheral arthritis and spondyloarthritis (SpA). Sterile osteomyelitis and chronic recurrent multifocal osteomyelitis (CRMO)—also known as chronic nonbacterial osteomyelitis (CNO)—may be prominent, especially in children. The cutaneous manifestations of SAPHO/CRMO/CNO are also rare and commonly include palmoplantar pustulosis (PPP) and nodulocystic acne, but other neutrophilic dermatoses are reported.

A recent survey of GRAPPA members found a wide range of treatments, reflecting the lack of trial evidence. The empirical treatment consists of nonsteroidal antiinflammatory drugs, colchicine, conventional synthetic DMARDs, bisphosphonates, and biologic drugs.[3] In the discussion, it was noted that very little is known about which primary cytokines drive these conditions. It was suggested that bone markers (such as procollagen peptide P1NP) be used as a measure of treatment response, though a valid imaging outcome is also required. It was noted that the Kahn criteria (Table 1) are commonly applied, but updates to the classification criteria for SAPHO/CRMO/CNO are needed.[4,5] Efforts are underway by Outcome Measures in Rheumatology (OMERACT) to develop core outcome sets in CRMO/CNO and SAPHO syndrome.

Drs. Callis Duffin and Helliwell presented and discussed several patient cases. Two patients were noted to have alopecia, which has not been commonly associated with SAPHO or CRMO/CNO. Both cases were associated with the use of TNFi to treat their musculoskeletal disease. The panelists noted that they had observed other cases of scarring and nonscarring alopecia in children and adults with CRMO/CNO and SAPHO syndrome and treated with TNFi; these usually resolved with topical corticosteroid use and/or switching to a different class of biologic. Another case triggered discussion on the role of needle aspiration of new bone lesions to rule out infection, which was controversial but must be strongly considered if a diagnosis of SAPHO syndrome has not been established.

3. Session With Dr. Arthur Kavanaugh and Dr. Joseph Merola

Hot topics in PsD were discussed in this session: the importance of Janus kinase (JAK) inhibitors for treatment of PsA, relevance of data regarding radiographic damage, and a review of topical agents for treatment of PsO.

Table 1. Diagnostic criteria proposed by Kahn and Kahn[4] in 1994[a].

1.	Chronic recurrent multifocal sterile osteomyelitis of peripheral or axial skeleton with or without dermatosis.
2.	Arthritis associated with PPP, pustular PsO, or severe acne.
3.	Any steroid osteitis associated with PPP, pustular PsO, or acne.

[a] Any of the criteria are diagnostic. PPP: palmoplantar pustulosis; PsO: psoriasis.

Several JAK inhibitors are currently approved in countries throughout the world for the treatment of rheumatoid arthritis (RA) as well as for PsA. Although there are many ongoing trials in skin PsO and other dermatologic conditions with promising early results, there are currently no licensed oral or topical JAK inhibitors for dermatologic indications.

JAK inhibitor safety, tolerability, and monitoring are of great importance to clinicians who care for people with PsD. Of particular relevance has been the recently available data in press releases from the ORAL surveillance study (A3921133; ClinicalTrials.gov: NCT02092467).[6] This trial evaluated the safety of tofacitinib (TOF) at doses of 5 or 10 mg twice per day compared to TNFi (adalimumab in the US and Canada; etanercept elsewhere) among 4362 patients aged ≥ 50 years with moderate-to-severe RA who had an inadequate response to methotrexate (MTX) and, importantly, ≥ 1 additional risk factor for cardiovascular (CV) disease. All entered the study on stable doses of MTX. The coprimary outcomes of the study were the incidence rates of malignancy (excluding nonmelanoma skin cancer) and major adverse cardiac events (MACE). In 2019, based on a review of the data by the study's Data and Safety Monitoring Board, the group receiving the higher dose of TOF was discontinued due to an imbalance in adverse outcomes, primarily deaths and venous thromboembolic events, in that group. More recently, adjudicated data for the 2 primary outcomes of the completed study were reported.

To assess statistical significance, the results for the TOF doses combined were compared to those for the TNFi arm. The rates of malignancy and MACE were numerically higher in the TOF groups, and the upper CI bound exceeded the prespecified criterion of noninferiority. Therefore, TOF was not considered as noninferior to TNFi therapy. The applicability of these safety data outside of a CV risk–enhanced RA population in other dermatologic and rheumatologic diseases remains to be determined. More thorough analyses of these data and data from other ongoing safety studies are eagerly awaited. Interestingly, there would appear to be lower concern for these safety issues around the pipeline of JAK inhibitors for topical use being assessed in indications such as vitiligo, alopecia areata, atopic dermatitis, and PsO.

Drs. Kavanaugh and Merola discussed the relevance and interpretation of data concerning the inhibition of progression of radiographic damage. It has been noted that dermatologists may value such data as an "insurance policy" that particular therapies are effective in ameliorating erosive, damaging PsA. This may also have implications for the phenotypes of those being selected to receive different targeted therapies. For example, individuals with known baseline erosions, damage, or more severe disease may be preferentially started on an agent known to address these aspects of PsA. However, it should be remembered that radiographic progression as observed in clinical trials has decreased in recent years, in part because the baseline degree of damage present is less and people are treated earlier in their disease course, making it harder to establish inhibition of progression.

Last, the presenters reviewed the robust pipeline of topical agents becoming available for the treatment of PsO, including nonsteroidal topicals such as tapinarof (aryl hydrocarbon receptor agonist) and roflumilast (topical phosphodiesterase-4 inhibitor). Given potential safety benefits, and the comorbidities affecting those with PsD, topical agents may emerge as a therapeutic option for more individuals with PsO. Topical agents may have a particular effect in areas of special interest, including scalp, inverse/intertriginous, genital, and facial locations of involvement.

4. Session With Dr. Philip Mease

In this session, a comparison of the axial disease domain of PsA (axPsA) with axial SpA (axSpA) was discussed, followed by a question-and-answer session.

Although it has long been known that there are subtle distinctions in the clinical manifestations of axPsA and axSpA, until recently it was not thought that such differences mattered regarding treatment response. If a medicine proved to be efficacious—or inefficacious—in clinical trials of axSpA, then it was assumed that similar results would be observed in axPsA, as exemplified by trials of TNFi and interleukin (IL)-17 inhibitors (IL-17i), which were shown to be effective for PsA. However, recent clinical trial data have forced a reconsideration of this assumption, and therefore a more careful examination of potential differences between these 2 conditions is warranted.

Previous studies of IL-23i medications showed no difference between the tested agent and placebo in ankylosing spondylitis (classified as radiographic axSpA). Although IL-23 is considered upstream of IL-17 in that it is produced upon IL-23 stimulation of IL-17–producing cells, it appears there may be immunobiologic differences, such as resident immune cells that release IL-17 independent of IL-23. A subset of participants in the 2 phase III PsA studies of guselkumab (NCT03162796, NCT03158285), an IL-23p1 inhibitor, deemed to have axPsA by the investigator and having evidence of sacroiliitis by radiograph or magnetic resonance imaging (MRI), were evaluated with clinical axSpA measures. Those treated with guselkumab demonstrated statistically greater improvement in measures such as Bath Ankylosing Spondylitis Disease Activity Index, spinal pain, and Ankylosing Spondylitis Disease Activity Score than placebo at 24 weeks and sustained benefit at 1 year. As a result of this exploratory posthoc analysis, a larger study devoted to patients with axPsA, including serial MRI evaluation of sacroiliac joints and spine, will be conducted to address whether the substudy findings were real (NCT04929210).

Could axPsA be different enough from axSpA such that an IL-23i could be effective in the former but not the latter? There are a number of genetic, clinical, and imaging characteristics that distinguish these 2 conditions. HLA-B27 gene positivity is seen in approximately 85% of patients with axSpA and 30% of those with axPsA. Other genes differ in the 2 populations. In axPsA, sacroiliitis may not be present or may present asymmetrically, unlike the majority of individuals with axSpA having sacroiliac inflammation and symmetry of involvement. Spinal syndesmophytes are often nonmarginal and "chunky" in axPsA, with "skip" areas and asymmetric involvement—different from the marginal, symmetric, and more uniform syndesmophytes of

axSpA. People with axPsA may not have symptoms of inflammatory back pain. Instead of symptoms appearing at an early age, in the beginning of the axSpA disease course, axPsA may appear at an older age, after other manifestations of PsA are already present. Because of the difficulty of obtaining tissue samples from the spine, it is difficult to study the immunobiology of axPsA. Noting the difference in clinical, genetic, and imaging features, it is not unreasonable to speculate that there could be differences between the immunophenotype of axPsA and axSpA, potentially allowing for differences in response to immunotherapies.

In addition to the guselkumab study in axPsA, there are several research initiatives underway to better understand this important clinical domain of PsA. The GRAPPA and Assessment of SpondyloArthritis international Society groups are collaborating on a study of at least 400 individuals with PsA in order to develop classification criteria for axPsA. A GRAPPA–Collaborative Research Network study to attempt to identify biomarkers to distinguish axPsA is also about to begin. Ongoing observations of individuals in clinical registries of PsA and axSpA will shed further light on the distinctions and similarities of these conditions.

5. Session With Dr. William Tillett and Dr. Maarten de Wit

In the final Meet the Experts session, the following topics were discussed: a review of composite measures in PsA, the challenges associated with composite measures, and assessment of disease activity in routine practice.

Dr. Tillett presented the current state of composite measures in PsA in clinical trials and routine practice. He emphasized the need for a continuous composite measure in PsA, encouraged by the voting from the GRAPPA 2019 annual meeting, where 90% of attending members supported such a measure.[7] The difference between response criteria and continuous composite measures was explained, including a summary of the existing measures: minimal disease activity (MDA), Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index, and Psoriatic Arthritis Disease Activity Score (PASDAS). GRAPPA members have previously voted that the PASDAS should be the preferred composite measure for clinical trials and MDA the target.[8]

Finally, Dr. Tillett described the challenges of composite measures in routine care. He discussed the relative merits of Routine Assessment of Patient Index Data, Disease Activity Score in 28 joints, composite DAPSA, and the 3- and 4-point visual analog scale (3-VAS and 4-VAS, respectively), reflecting the voting from previous GRAPPA meetings. The 3-VAS and 4-VAS scores have been proposed as feasible tools for routine care with separate measurement by physician and patients.[9] Initial data suggested the 3-VAS (physician global [PGA] + patient global + patient skin assessments) and 4VAS (PGA + patient pain + patient joint + patient skin assessments) have superior effect sizes, responsiveness, and associations with treatment change; further testing is underway.[9]

Discussion focused primarily on the assessment of disease in routine clinical practice and the patient perspective. Dr. de Wit commented that the 3-VAS and 4-VAS scores are patient-centered tools but asked if the PGA was still required and whether it was old fashioned to use. Dr. Tillett suggested that in the absence of a single perfect measure, there was a need to triangulate the truth of disease state using multiple assessments from different sources (patient, physician, laboratory, and imaging). Prof. Adebayo posed the question, "Whose target is this anyway?" suggesting that a composite measure is a medical/academic construct. There is a need for a patient-centered outcome, such as an ability to perform certain tasks (eg, hug a grandchild). Prof. Adebayo said the disconnect between physician and patient outcomes applied to all outcomes and advocated for simple tests; for example, the button test (the ability to undo/do up a button). As a patient research partner (PRP), Dr. de Wit commented that he was a "big supporter" of composite measures, suggesting they could be the best of both worlds—a comprehensive assessment of disease activity and effect. However, rather than just relying on the final score, the clinician and patient should interpret individual components of the composite measure (such as skin and joint disease or effect of disease in the Psoriatic Arthritis Impact of Disease [PsAID]) to facilitate the clinical interaction.

The attendees agreed the PsAID was a useful tool for assessing effect of disease in clinical trials and clinical practice alongside measures of disease activity. Prof. Niti Goel (also a PRP) commented that the concept of the PGA can be challenging, the numeric rating scale has superior psychometric properties to the VAS, and measurement with any tool does not obviate the need for other assessments (eg, the physical exam or imaging). Prof. FitzGerald commented that the PGA may be an old-fashioned term in the modern era of multidisciplinary care, and that perhaps "clinician assessment" may be more appropriate. Prof. Vinod Chandran noted the discrepancy of measuring disease in the acute setting (hospital) with no information between visits. He suggested that we need to move assessment out of hospital and toward regular measures, which may include remote PROMs, smartphone/accelerometer data, and blood tests.

Conclusion

The GRAPPA community greatly appreciated the scientific contributions of the rheumatology and dermatology experts on PsD and the interesting discussions that followed.

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