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GRAPPA Treatment Recommendations: 2021 Update

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ABSTRACT. Since its inception, one of the central missions of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) has been the development of treatment recommendations for patients with psoriatic arthritis (PsA). The initial guidelines, developed in 2009, were updated in 2015. Because of the abundance of new data concerning the therapeutic approach to PsA, GRAPPA members have been working throughout 2020–2021 to once again update the recommendations. At the GRAPPA 2021 annual meeting, the full committee presented proposals from each of the treatment domain groups, including the comorbidities and related conditions groups, based on previous systematic literature reviews. Overarching principles and summary evidence tables were presented, including results from a GRAPPA membership survey of patients and clinicians to assess levels of agreement. A draft of the figure for the treatment recommendations was presented and discussed with the wider membership.

Key Indexing Terms: GRAPPA, psoriasis, psoriatic arthritis

Introduction

Significant advances in novel therapies and new evidence on treatment strategies in psoriatic arthritis (PsA) necessitate regular updates to treatment recommendations. The first iteration of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) treatment recommendations was in 2009.[1] In 2019, GRAPPA started the process to update the 2015 GRAPPA treatment recommendations, and these are now being finalized.[2] Most newer iterations of treatment recommendations have adopted methods such as Grading of Recommendations Assessment, Development, and Evaluation (GRADE) to ensure a transparent approach to grading the evidence. This paper presents the results of discussions during the virtual GRAPPA 2021 annual meeting with the aim of collecting feedback on the various proposed treatment domain recommendations.

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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Discussion Topics

Underpinning evidence review. A wide-ranging evidence review was used to update the 2015 guidelines.[2] The systematic searches and methodology aiming to identify randomized controlled trial (RCT) data across multiple domains of PsA have previously been reported.[3]

Additional searches of RCTs and other studies (nonrandomized controlled studies, cohort studies, and pre-post studies) were completed for the 2 groups, addressing conditions commonly associated with PsA (ie, inflammatory bowel disease [IBD] and uveitis), as well as for other comorbidities. These searches addressed (1) treatment options in patients with PsA and comorbidities, (2) RCTs of individuals with IBD or uveitis treated with pharmaceutical drugs used in PsA, (3) screening of comorbidities and related conditions in PsA, and (4) prognosis and phenotype of individuals with PsA and related conditions.

Overarching principles and additional guidance statements. Overarching principles for the management of people with PsA were included in the 2015 version of the GRAPPA recommendations. These have been updated to incorporate new evidence-based principles and experience-based approaches for goals of treatment. One additional overarching principle has been included to highlight the optimal role of the recommendations within a shared decision-making approach, and 2 additional position statements were added, covering biosimilars and tapering therapy. In May 2021, the overarching principles and guidance statements were circulated to the wider GRAPPA membership for agreement voting. High levels of support (> 80% in most cases) were identified both from patient research partners (PRPs) and from GRAPPA clinicians.

Evidence table and treatment recommendations. Following the evidence review, all the individual domain groups contributed to a proposed summary evidence table (Table 1). The table followed a GRADE format, resulting in strong/conditional

Table 1. Proposed summary evidence table skeleton for treatment recommendations for PsO.

Indication	Strong Recommendation For	Conditional Recommendation For	Conditional Recommendation Against	Strong Recommendation Against	Unclear
Peripheral arthritis, DMARD-naïve					
Peripheral arthritis, DMARD inadequate response					
Peripheral arthritis, biologic-experienced					
Axial arthritis, biologic-naïve					
Enthesitis					
Dactylitis					
PsO, plaque					
Nail PsO					
IBD, Crohn disease					
IBD, UC					
Uveitis					

DMARD: disease-modifying antirheumatic drug; IBD: inflammatory bowel disease; PsO: psoriasis; UC: ulcerative colitis.

recommendations either for or against a drug. This was developed with consensus across all group leaders and will be presented elsewhere.

Methodology. To aid in consistency, several topics that could potentially be interpreted in different ways by different groups were considered. First, individual drugs with an ostensibly shared mechanism of action would be considered as one group unless there was solid evidence for within-class differences (eg, the 5 distinct inhibitors of tumor necrosis factor [TNF] are grouped as TNF inhibitors [TNFi]; calling out evidence-based differences, such as the inefficacy of etanercept in IBD). Second, the methods aimed to use data from PsA studies, although for some domains such as uveitis and IBD, the majority of the data come from studies outside of PsA. Third, the goal was not to provide primary recommendations for the treatment of these associated conditions (eg, IBD), but rather to serve as a resource for consideration of approaching active disease within these domains for patients with PsA. Fourth, as GRAPPA guidelines are international, and as regulatory approvals can vary substantially in different jurisdictions, specific licensing or regulatory language from any individual area were not considered to be evidence; instead, data from the published research trials formed the basis of the recommendations.

Discussion at the 2021 Meeting

Following a presentation from each of the domain subgroups, the proposed summary table and a draft of the planned figure were presented for discussion. Questions were invited from GRAPPA members and answered by the committee.

1. *Is there parity where multiple drugs are recommended?* In the proposed summary table, drugs with positive evidence within a particular domain of disease are listed, but in no particular order. There is limited evidence comparing therapies in PsA, but in certain domains, head-to-head trials have shown superiority for one drug over another.

2. *Why are Janus kinase inhibitors equally recommended for axial disease when evidence for axial PsA (axPsA) and axial spondyloarthritis (axSpA) are limited?* As noted, individual drugs with an ostensibly shared mechanism of action would be considered as a group in the absence of solid evidence for within-class differences. There is now one large RCT addressing axPsA specifically with 1 Janus kinase inhibitor, but most recommendations are extrapolated from studies in ankylosing spondylitis or axSpA.

3. *What types of psoriasis (PsO) do the recommendations address?* The recommendations for skin PsO refer specifically to plaque PsO, as there is a paucity of data on other PsO phenotypes (eg, pustular PsO).

4. *Why are corticosteroids not included in treatment of uveitis?* The recommendations are not meant to be applied as primary treatments for uveitis, but rather to act as guidance. We would always recommend that management of related conditions should be discussed with appropriate specialists.

5. *How do you propose that we treat patients who present with multiple domain involvement?* This speaks to the core principle of the proposed figure; namely, a clinician using these recommendations should fully assess disease activity across individual domains in order to ascertain the effects of treatment on each patient. Then clinicians can identify which drugs are efficacious in those particular domains and provide this information to the patient.

6. *Will there be any recommendation on concomitant methotrexate with biologics?* Discussions around concomitant conventional synthetic disease-modifying antirheumatic drug (csDMARD) use alongside biologics is not included in the table or figure but will be covered in the text of the recommendations. Since 2015, additional data are available on the use of concomitant DMARDs for efficacy (eg, the SEAM-PsA study) and for persistence of TNFi specifically (from registry data).

7. Will there be any distinction between primary and secondary inefficacy for the selection of second-line therapy? Again, this will be discussed in the text, although limited data exist, particularly in RCTs, and there is no clear definition of primary and/or secondary failure. While the concepts seem straightforward, in reality "failure" of any treatment can be much more complex, necessitating the consideration of efficacy across various

domains over time, tolerability issues, and exogenous factors such as cost.

8. Will there be any recommendations on measuring drug trough levels? Therapeutic drug monitoring has been raised as a topic of consideration; however, the limited data published to date do not support its regular use in PsA.

9. Is there a plan to update the PRP treatment recommendations? Have people used the previous document with their patients? The clinicians on the panel replied they had used the previous iteration for their clinics. The patient representative (DO) replied that he was keen to update the PRP treatment recommendations in parallel with the main recommendations.

Conclusion

GRAPPA is currently finalizing domain-specific recommendations with an aim to produce updated treatment recommendations for publication in 2022. These follow a GRADE-informed methodology to update recommendations, taking account of the strengths and limitations of the evidence base. There has been strong agreement with the recommendations identified in GRAPPA membership polls throughout development.

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