GRAPPA Treatment Recommendations: An Update from the GRAPPA 2014 Annual Meeting and GRAPPA Meeting Adjacent to the 2014 ACR Meeting

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ABSTRACT. At the 2014 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), members discussed an update of their previous treatment recommendations published in 2009. Domain subcommittees representing the different aspects of psoriatic arthritis (PsA) had been reconvened in 2013 and a new group was formed that focused on PsA comorbidities and associated conditions. A combined literature review was completed in February 2013 followed by individual group literature reviews and analyses. Articles from each of these subcommittees were published in 2014, updating the evidence for individual therapies in PsA. At their 2014 annual meeting, GRAPPA members discussed their plans for a summary article on treatment recommendations, finalized the Grading of Recommendations Assessment, Development and Evaluation (GRADE)-formatted recommendations for individual drugs within the domain subcommittees, and presented these for debate. Modifications to the GRAPPA grid were also discussed in breakout groups and presented to the full membership. At the GRAPPA meeting adjacent to the 2014 American College of Rheumatology meeting, a new GRAPPA treatment schema was proposed to replace the original GRAPPA grid. Each domain subcommittee discussed treatment algorithms based on their GRADE recommendations for inclusion in the final treatment recommendations article, which will be submitted in 2015. (J Rheumatol 2015;42:1052–5; doi:10.3899/jrheum.150132)

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A central mission of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) is to develop recommendations for the optimal treatment of patients with psoriatic arthritis (PsA)[1]. In 2013, GRAPPA members initiated an update of their previous treatment recommendations published in 2009[2]. Six domain subcommittees were reconvened, a new group was formed to focus on PsA comorbidities and associated conditions, a combined literature review was completed, and the results were disseminated to the subcommittees for review and analysis. Subcommittees also performed additional literature searches within their domain. Articles from each of these groups have now been published, appraising the evidence for individual therapies in PsA[3,4,5,6,7,8,9].

Prior to the GRAPPA 2014 annual meeting, a number of overarching principles to be included in the new treatment recommendations were developed from discussion at the European League Against Rheumatism (EULAR) and with key members of the subcommittees. These principles were circulated to members in an online survey to solicit feedback in June 2014.

GRAPPA 2014 Annual Meeting, New York, New York, USA

Results of the online survey of the overarching principles were presented at the annual meeting in New York and changes were incorporated into their wording. Unfortunately, despite the intention to include the GRAPPA patient members in the overall survey, for technical reasons patient research partners (PRP) did not receive the survey. PRP attending the New York meeting participated in the plenary discussion on the overarching principles.

Following the presentation of overarching principles at the annual meeting, all industry members were dismissed. All other GRAPPA members then joined breakout groups based on the following domains: peripheral arthritis, skin, nails, dactylitis, enthesitis, axial disease, and comorbidities. Each

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group was asked to formulate GRADE (Grading of Recommendations Assessment, Development and Evaluation[10]) recommendations for each individual treatment (e.g., drug) or class of drugs within their subgroup, based on the evidence generated in the literature reviews. At least 1 PRP was present in each group. Initially, groups decided on the most relevant clinical situations that needed to be addressed within domains. These formed the PICO (population, intervention, comparator, outcome[11]) questions of whether one or another particular treatment should be recommended for use in a specific clinical scenario, and the level of recommendation based on the GRADE system (i.e., strong or conditional). These recommendations will be included in a summary treatment recommendations manuscript, with the PICO questions and data planned to be included as supplementary material. The recommendations were presented in a GRADE format and reported by the domain groups to the other members at the conference. During a feedback session, all members were encouraged to comment on and debate the recommendations for the individual drugs.

Breakout groups were also asked to consider the GRAPPA treatment grid, which was developed as part of the 2009 treatment recommendations and included measures defining mild, moderate, and severe disease activity in each domain. Groups reviewed the measures and the cutpoints for defining disease activity and were asked to provide input on assessments for disease activity. Most breakout groups proposed changes to the GRAPPA grid. A number of them discussed the difficulty of defining a cutpoint between moderate and severe disease; they suggested instead that definitions be limited to 2 categories: mild disease and a single category of moderate/severe disease. Other concerns were voiced regarding the specific cutpoints and measures: evidence is lacking to support specific cutpoints for disease activity in the PsA literature; and in many domains, the optimal outcome instruments to assess disease activity have not been established. Concerns were also raised about the heterogeneity of presentation in PsA and the difficulty of defining cutpoints appropriate for all patients. This point was also considered key by the dermatologists when considering their "typical" patients with more severe skin disease. The nail domain group also requested that nails be separate from the skin domain given that outcome measures and therapies may differ from skin.

Finally, to develop a treatment algorithm in the individual domains, breakout groups were asked to consider both the GRADE recommendations for individual drugs and the GRAPPA grid defining disease activity.

Some discussion also concerned how evidence gathered by the comorbidities group should be incorporated. One suggestion was that this could be a filter following the grid that could lead to either escalation of therapy if the presence of other related conditions such as inflammatory bowel disease was identified, or a reduction or change in therapy if potential contraindications to therapy such as liver disease or cardiovascular disease were identified.

The work from the New York meeting was followed by discussions at the American College of Rheumatology (ACR) meeting in Boston, Massachusetts, USA, in November 2014.

GRAPPA Adjacent to the 2014 ACR Meeting

Many rheumatologist members of GRAPPA attending ACR 2014 participated in a satellite session to further develop the treatment recommendations. Additional changes to the overarching principles were made, with a final draft discussed further by teleconference with 2 PRP from the peripheral arthritis subcommittee after the meeting before dissemination to the full membership for input and consensus. Debate was particularly strong over the wording of Principle 5 regarding therapeutic decisions. Physicians and PRP debated whether wording should suggest a joint decision on treatment by physicians and patients or if the ultimate decision should be made by the patient. Everyone was keen to recognize the importance of patient preferences while acknowledging that some therapies may be contraindicated in some patients. The final wording for circulation now states: "Therapeutic decisions need to be individualized, and are made jointly by the patient and their doctor. Treatment should reflect patient preferences, with the patients having had the best information and relevant options provided to them. Treatment choices may be affected by various factors, including the comorbid conditions outlined above, previous therapies tried, and other factors." A final online survey to establish levels of agreement of the membership with these principles was circulated in January 2015 to allow inclusion of these data in the treatment recommendations article.

A new proposal to replace the GRAPPA grid was presented to the members at the meeting. This new treatment schema (Figure 1) includes the 6 domains of disease activity (joints, skin, nails, enthesitis, dactylitis, and axial disease), and each domain is graded as active or inactive, rather than using set cutpoints to define disease activity levels. Active disease is defined as signs and symptoms that are viewed as unacceptable to the patient and that are determined to be related to PsA by the doctor. Each domain group was then asked to create a flowchart to designate treatment options based on their drug recommendations at the 2014 GRAPPA meeting. This new flowchart first assesses the patient for activity in the different domains of involvement and identifies previous therapies, and then considers other factors, including patient preference, presence of comorbidities, and/or related spondyloarthritis conditions. Potentially, treatment could be "escalated" at this point if other related conditions are also active, such as inflammatory bowel disease or uveitis. Conversely, therapy may be contraindicated or at least less suitable if certain comorbidities such as liver problems or cardiovascular problems are present.

The wording of the new flowchart was debated at the

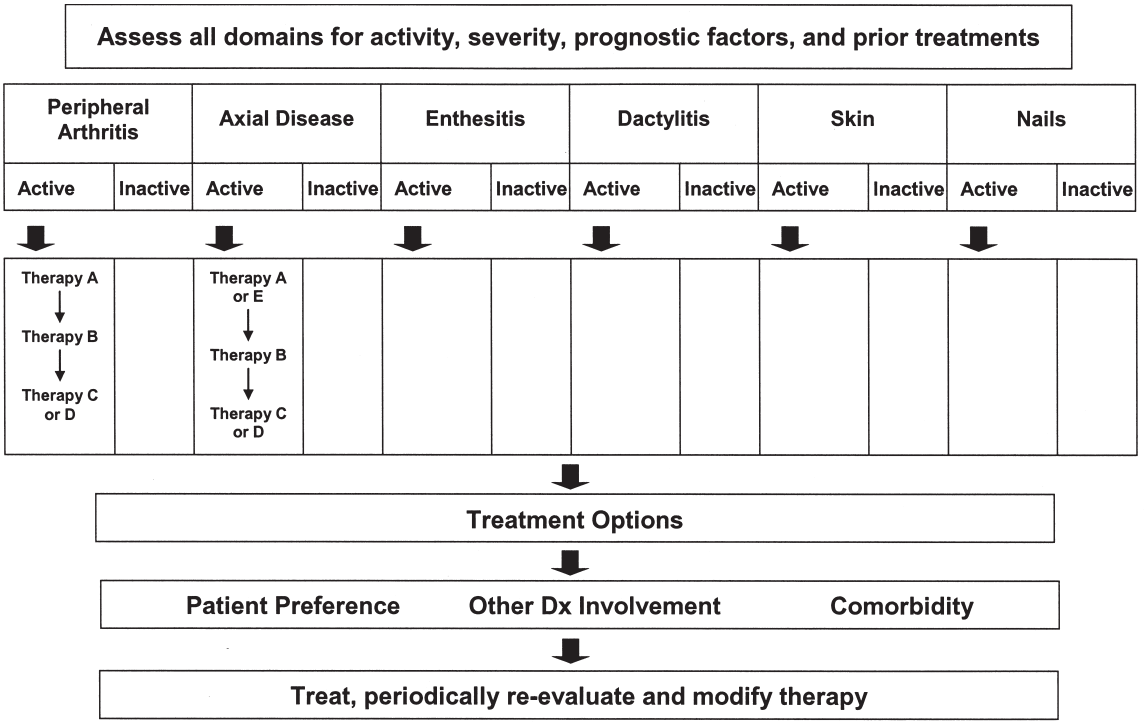

Figure 1. GRAPPA treatment recommendations schema.

Boston meeting. The step of considering previous therapies was added. Overall, the members in attendance were in favor of the simplified flowchart because it is more easily adaptable to individual patients and avoids non-evidence-based and prescriptive cutpoints for different levels of disease activity.

Following this initial group discussion, each of the domain groups (except for skin and nails: dermatologists were not present) formed breakout groups to discuss their treatment suggestions to populate the overall flowchart. It was suggested that when a clear order of therapies was identified (first line, second line, etc.), this sequence should be shown. However, when therapies were found to be equivalent in terms of efficacy and safety, they could be listed on the same line.

Final discussion at the ACR Boston meeting related to plans for completing the treatment recommendations. Because dermatologists were not in attendance, it was planned that their input would be obtained before the American Academy of Dermatologists Meeting in March 2015, after which the final manuscript could be completed.

The groups decided to update their literature reviews to November 2014 to ensure that all relevant evidence was included. A lively debate ensued about the inclusion of evidence from conference abstracts, with particular concerns about evidence that had not been peer-reviewed and published in a full-length report. Also, some therapies included in the review of evidence have not been approved and may never gain approval in certain countries. Many of the members, however, said that limiting the review to published literature may result in dissemination of recommendations that would become outdated given the rapid pace of drug development in PsA and the high likelihood that abstracts of large, high-quality phase III studies would be published as full-length reports in the near future. Based on these considerations, the majority of members agreed by a formal vote that data from abstracts also should be considered in the development of the recommendations, but given less weight than evidence from published reports. It was also agreed that data derived from abstracts should be differentiated from data abstracted from published clinical trials or observational studies. These abstract data will be clarified in the text of each subcommittee's recommendations, and any recommendations based on abstract data alone will be clearly identifiable (in gray text) within the treatment schema.

Next Steps

Following the New York and Boston meetings and the final survey, the recommendations task force will make sure that the patient perspective will be incorporated in the final version of the overarching principles. The individual domain groups are finalizing their recommendations to populate the overall flowchart, including the skin and nail groups who will be doing this remotely. The GRAPPA treatment recommendations should be finalized in the first quarter of 2015 with a view to presenting a version of them at the EULAR 2015 congress.

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