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TITLE: Expert consensus on a set of outcomes to assess the effectiveness of biologic treatment in psoriatic arthritis: the MERECES study

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ABSTRACT

Objectives: To reach a consensus on the instruments to be used in clinical practice to evaluate the effectiveness of biological disease-modifying antirheumatic drugs (bDMARD) treatment in PsA patients in the short-medium term (3-6 months), and to establish the minimum health outcomes for treatment continuation.

Methods: A two-round Delphi questionnaire was developed based on both the information gathered in the literature review and four discussion groups. The suitability and feasibility of the proposed sets of instruments were assessed on a 7-point Likert scale. Consensus was established when at least 75% of healthcare professionals (HCPs) reached agreement. To define a minimum health outcome in order to continue treatment a combination of four disease activity states and three health-related quality of life states were defined for three hypothetical patient profiles. HCPs were given a dichotomous choice ("yes/no") in response to whether they would continue treatment in each case.

Results: 106 HCPs completed the second round. Consensus was reached on the use of: 1) Disease Activity in Psoriatic Arthritis (DAPSA) + Psoriatic Arthritis Impact of Disease (PsAID-12) or Minimal Disease Activity (MDA) + PsAID-12 + C-reactive protein, in peripheral PsA; and 2) Ankylosing Spondylitis Disease Activity Score (ASDAS) + PsAID-12, in axial PsA. Health outcomes considered sufficient to continue treatment were stricter for bDMARDs-naïve patients than for patients who failed several bDMARDs.

Conclusions: To the best of our knowledge, this is the first multi-disciplinary consensus on a set of outcomes for the evaluation of bDMARDs effectiveness in PsA, in routine clinical practice.

1. INTRODUCTION

Psoriatic arthritis (PsA) is a chronic musculoskeletal disease characterized by heterogeneous manifestations such as arthritis, spondylitis, dactylitis, enthesitis and/or psoriasis. Nearly 70% of PsA patients develop skin lesions prior to the onset of arthritis, 15% develop musculoskeletal symptoms first, while both symptoms coexist in the other 15%(1). Symptom burden, in turn reduce work productivity and increase healthcare costs, particularly in patients with severe PsA(2–6). Therefore, health-related quality of life (HRQoL) is commonly impaired in these patients. The most frequent presentations of PsA are peripheral oligo-articular and symmetrical polyarticular arthritis. However, both axial and peripheral involvement may coexist(7)..

Current therapies aim to prevent the progression of structural damage, maintain functional status and improve HRQoL(8). Development of new biological disease-modifying antirheumatic drugs (bDMARDs) has improved disease management and provided better patient care. However, complete disease control has not yet been achieved(7,9).

Given the complexity of PsA, a holistic approach is required to assess the effectiveness of treatment(10). The combined use of clinical outcomes and patient reported outcomes (PROs) in clinical practice is a pragmatic way of gaining a comprehensive view of patient well-being (11). The group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and the group for Outcome Measures in Rheumatology (OMERACT) have jointly developed a core domain to be measured in randomized controlled trials (including both clinical outcomes and PROs). Eight mandatory domains ("inner core": musculoskeletal disease activity, skin disease activity, pain, patient global, physical function, HRQoL, fatigue and systemic inflammation) and four strongly recommended but non-mandatory domains ("middle circle": participation, economic costs, structural damage and emotional well-being) were established(10,12). In addition, four domains ("outer circle ") were suggested to be further explored in the future.

The GRAPPA-OMERACT has defined remission or alternatively low disease activity/minimal disease activity as treatment target(13). Nevertheless, no consensus was reached on which measures are more appropriate to assess the disease activity. This lack of consensus is of particular importance given the great heterogeneity of existing instruments(13,14) which hinders the holistic and standardized evaluation of treatment effectiveness(15,16).

The MERECES group (in Spanish: *MEdir Resultados. Consenso de Evaluación en Salud para artritis psoriásica*) aims to reach a consensus on the instruments to be used in clinical practice to

evaluate the effectiveness of bDMARD treatment in PsA patients in the short-medium term (3-6 months) and to establish the minimum health outcomes for treatment continuation.

2. METHODS

The study comprised three phases: (1) literature review -June 2017-; (2) discussion groups with patients and healthcare professionals (HCPs) -January and February 2018; (3) Delphi consultation -May and July 2018- (Figure 1).

The project was led by a multidisciplinary steering committee consisting of three rheumatologists with experience in PsA management, one methodologist and one healthcare manager.

2.1. Literature review

A literature review was conducted using the international databases (MedLine/PubMed, Google Scholar, Cochrane library e ISI-WOK) to identify clinical outcomes and PROs, and their measuring instruments, for the follow-up of PsA patients. It included clinical trials, PsA-related observational studies and literature reviews published in English or Spanish until June 2017.

2.2. Measurement properties of PROMs

Prior to the HCP discussion group, Patient Reported Outcome Measures (PROMs) identified in the literature review were pre-selected based on the availability of a validated transcultural adaptation for Spanish patients (if required), number of core domains covered, feasibility of use in clinical practice (≤25 items) and psychometric properties (consistency reliability, test-retest reliability, responsiveness and minimal importance difference). No pre-selection of clinical instruments was undertaken.

2.3. Discussion groups

Four discussion groups were conducted according to the information extracted in the literature review: two with PsA patients (n=15) and two with HCPs (including rheumatologists, hospital pharmacists, nurses, clinical psychologists and healthcare managers; n=19).

PsA patients (diagnosed more than 6 months earlier) on biological treatment (for at least 3 months) were invited to participate by the national patient advocacy group "Acción Psoriasis". In order to obtain representatives of the different PsA phenotypes, patients were selected based on their sociodemographic (age and gender) and clinical characteristics (joint disease and skin manifestations, time since diagnosis, time since treatment onset). The main objective of discussion groups was to explore and identify the most relevant health outcomes and their

measuring instruments based on the patient's perspective. In addition, a second objective was to explore patients' willingness to complete questionnaires to assess PROMs.

Health care professionals (HCPs) were selected according to their professional experience and interest in the project. The objective of HCPs' discussion groups was to identify the most appropriate outcomes and the corresponding measuring instruments, to evaluate the effectiveness of bDMARDs in routine clinical practice. HCPs were asked to define several sets of instruments to take clinical outcome measures and PROMs to be included in Delphi questionnaire.

2.4. Delphi consultation

The Delphi technique is widely used to achieve a consensus, and allows anonymity between participants and controlled feedback(17,18). In order to obtain agreement on the assessment of treatment effectiveness two Delphi rounds were planned.

A Delphi questionnaire was developed based on both the information gathered in the literature review and discussion groups. The first-round questionnaire consisted of three sections: (1) Sociodemographic and occupational characteristics of participants. (2) Instrument suitability. It was assessed on a 7-point Likert scale (from "1=completely disagree" to "7=in total agreement"). (3) Suitability and feasibility of using the instrument sets proposed for patients, with axial or peripheral involvement in routine clinical practice. The suitability and feasibility of the sets were assessed on a 7-point Likert scale (from "1=completely disagree" to "7=in total agreement").

Consensus was established when at least 75% of respondents reached agreement 1-3) or disagreement 5-7).

The second-round of the questionnaire was composed of two sections: (1) Prioritization of agreed instrument sets in the first-round and (2) definition of a minimum health outcome to be achieved in a short-medium term (3-6 months) in order to continue treatment. In this section, we defined a combination of four disease activity states [remission, low activity, and moderate/high activity with and without clinically important improvement (CII)] and three HRQoL states (optimal HRQoL and suboptimal HRQoL with and without CII) for three hypothetical patient profiles: (A) bDMARDs-naïve patient with PsA; (B) PsA patient without structural damage, and/or functional disability, and/or mild-moderate psoriasis and failure to respond to one bDMARD; (C) PsA patient with structural damage, serious sequelae and failure

to respond to several bDMARDs. Panelists were given a dichotomous choice (yes/no) in response to whether they would continue treatment in each case.

PsA patients achieving remission and optimal HRQoL should continue treatment. This scenario was considered as a test to identify panelists who did not understand the second part of the questionnaire. Therefore, panelists who considered that patients should not continue treatment on achieving remission with optimal HRQoL were excluded from the analysis.

2.4.1. Delphi panelists

There is no agreement in the literature on the appropriate number of panelists for the Delphi method, although a sample of 23 experts has been suggested sufficient(19). We planned to obtain a sample size of 80 panelists. Assuming a potential loss of 50%, a total of 162 panelists were invited to participate in the consultation. They were selected by the promoter and the scientific committee based on their professional experience in PsA management and interest in the project. A minimum of 2 years' professional experience was required. Panelists received by email the link to the questionnaire, username and password (unique for each participant). HCPs who participated in the discussion groups (n=19) as well as other rheumatologists and dermatologists (n=143) were invited. Due to the nature of the questionnaire, which required specialized clinical knowledge of the disease, patients were not invited to participate as Delphi panelists.

2.5. Data analysis

Frequencies and percentile distributions were calculated for each option using STATA statistical software, version 14.

2.6. Ethics

The study was approved by the Research Ethic Committee of Asturias (nº229/17). All participants received adequate information on the study and agreed to participate by signing an informed consent. To ensure data confidentiality, all documents were duly encoded.

3. RESULTS

3.1 Literature review

A total of 138 publications were reviewed. These publications described 87 instruments used for PsA patient's follow-up (43 PROMs, 32 clinical instruments and 12 composite indexes). None of the identified instruments assessed all eight core domains established by the GRAPPA-OMERACT group.

The composite indexes that assess the most core domains are: Assessment of SpondyloArthritis International Society (ASAS) criteria (5 domains), Minimal Disease Activity (MDA) (5 domains), American College of Rheumatology criteria (ACR) (4 domains), Ankylosing Spondylitis Disease Activity Score (ASDAS) (4 domains), Disease Activity in Psoriatic Arthritis (DAPSA) (4 domains) and Psoriatic Arthritis Disease Activity Score (PASDAS) (4 domains).

The psychometric properties of pre-selected PROMs presented to HCPs are showed in the appendix table.

3.2 Patients discussion groups

A heterogeneous group of 15 PsA patients participated in two discussion groups. The sociodemographic and clinical characteristics are presented in Table 1.

Patients considered impairment of physical, as well as emotional well-being, to be the most important aspects. In fact, most of them requested psychological support due to the impact of both arthritis and psoriasis. Nonetheless, different opinions were observed according to the severity of arthritis and psoriasis-related symptoms.

The use of PROMs in clinical practice was found valuable for PsA management. However, according to the patient's experience, its use was limited and determined by the particular hospital and Spanish region where the patient received treatment. Participants indicated their willingness to complete PROMs not exceeding 15 items at every medical check-up.

3.3 HCPs discussion groups

A multidisciplinary group of 19 HCPs (5 rheumatologists, 4 hospital pharmacists, 2 dermatologists, 2 psychologists, 2 nurses and 4 healthcare managers) participated in two discussion groups.

Participants considered the eight "core domains" defined by GRAPPA-OMERACT for the evaluation of PsA patients to be essential. With respect to the four "middle circle domains" , participants considered participation and emotional well-being relevant but discarded structural damage and economic cost. Structural damage was dismissed because it is irreversible, and its progression is unmeasurable in the short-term. Economic cost was not selected as it was considered unsuitable for evaluating treatment effectiveness. The four "outer circle domains" were not considered because they have not been sufficiently established. Therefore, participants agreed to assess 10 out of 16 domains by combining validated composite indexes

and PROMs. Considering the different manifestations of axial and peripheral involvement, specific composite indexes were proposed for each one.

3.3.1. Instruments to evaluated disease activity in PsA patients

Participants selected ASDAS to evaluate axial involvement because it allows for direct measurement which is easily implemented in clinical practice. The reasons for selecting DAPSA for the peripheral PsA evaluation included its responsiveness, simplicity of calculation and usage, and ability to evaluate 66/68 joints. Furthermore, DAPSA correlated with function and radiographic progression(20). It was argued that the 28 joint counts do not necessarily capture commonly affected joints in PsA, such as distal inter-phalangeal hand joints, and feet joints. For this reason, DAS28, as well as other composite indexes evaluating 28 joints, was discarded. MDA was considered as an alternative for both peripheral and axial PsA, since MDA is the only composite index evaluating skin disease. Nonetheless, it was noted that MDA is not a measure of disease activity and does not assess acute phase reagents such as the C-reactive protein (CRP).

3.3.2. Instruments to evaluate HRQoL in PsA patients

In relation to PROMs, PsAID-12 (hereinafter referred to as PsAID) was the only PsA-specific multi-domain HRQoL questionnaire found. It is a reliable instrument, developed and validated by the European League Against Rheumatism (EULAR) for its use in clinical practice, covering most core and "middle circle" domains(21). HCPs agreed to use PsAID rather than DLQI since the latter only assesses skin involvement.

3.3.3. Sets of instruments

Finally, three sets of instruments were proposed to reach a consensus in Delphi consultation: 1) DAPSA + PsAID; 2) MDA + PsAID + CRP; 3) ASDAS + PsAID. Sets 1 and 2 were presented to patients with peripheral involvement and sets 2 and 3 were implemented for patients with axial involvement.

3.4. First- round Delphi consultation

3.4.1. Sociodemographic and occupational characteristics of participants

HCP, who participated in the discussion groups (n=19), and other rheumatologists and dermatologists (n=143) were invited to participate. A total of 115 panelists with a mean PsA management experience of 21.7 years (DE: 19.3), representing almost all Spanish regions, completed the first-round questionnaire (response rate 70.9%). Sociodemographic characteristics of the participants are described in Table 2.

3.4.2. *Instrument suitability*

Most of participants considered that both composite indexes DAPSA (89.6%) and MDA (91.3%) were useful to evaluate the efficacy of bDMARDs in patients with peripheral involvement whereas only ASDAS was considered useful (90.4%) in patients with axial involvement. PsAID was considered a useful PROM to assess the impact of PsA on HRQoL in patients with both peripheral (83.5%) and axial (76.5%) involvement.

3.4.3. *Suitability of sets and feasibility of their use in routine clinical practice*

In patients with axial involvement, consensus was reached on the use of ASDAS + PsAID [Agreement on suitability (S) 85.3%; Agreement on feasibility (F): 86.9%] but not on the use of MDA + PSAID + CRP (S: 69.6%; F: 76.5%). In patients with peripheral involvement, consensus was reached on the use of either DAPSA + PsAID (S: 91.4%; F: 85.2%), or MDA + PsAID + CRP (S: 90.5%; F: 76.5%).

3.5. Second-round Delphi consultation

One hundred and six HCPs completed the second-round questionnaire (response rate from the first-round 92.2%).

3.5.1. Set prioritization

For peripheral PsA, DAPSA + PsAID were prioritized over MDA + PsAID + CRP (72.6% vs. 27.4%).

3.5.2. Health outcomes to qualify for treatment continuation

Responses from 97 participants who answered the test scenario properly were analyzed. Panelists agreed that bDMARDs-naïve patients with PsA (profile A) should achieve at least low activity (defined as DAPSA ≤14 or ASDAS ≤2.1) and CII on HRQoL (established as PsAID Δ ≥3) within 3-6 months of starting treatment to continue the bDMARDs. Experts were less strict in the case of PsA patients lacking structural damage, and/or functional disability, and/or mild-moderate psoriasis, and failure to respond to one bDMARDs (profile B). In this respect, they reached a consensus on continuing bDMARDs when patients achieved low activity and CII on HRQoL, or remission (defined as DAPSA ≤4 or ASDAS ≤1.3) regardless of the HRQoL. Finally, experts agreed to continue treatment when PsA patients with structural damage, serious sequelae and failure to respond to several bDMARDs, achieved low activity (independent of HRQoL), or moderate/high activity with CII (defined as DAPSA Δ≥85% or ASDAS Δ≥1.1) and optimal HRQoL (established as PsAID ≤4) within 3-6 months of starting treatment (Table 3).

4. DISCUSSION

The assessment of treatment efficacy in a holistic and standardized approach is challenging in PsA. The main hurdles include heterogeneity of PsA manifestations, transition between phenotypes during disease course, and the wide variety of instruments available(16,22–24). Currently, Spanish rheumatologists are not following specific criteria to assess the response to biologic therapies in patients with PsA. To some extent, this is due to the absence of specific recommendations in the main national guidelines, such as the one developed by the Spanish Society of Rheumatology(25). In the present study, the MERECES group has reached a consensus on the instruments to be used in clinical practice for the evaluation of bDMARDs effectiveness (in 3-6 months), in patients with PsA. In addition, experts have agreed on the use of both clinical outcomes and PROMs in line with the GRAPPA-OMERACT recommendations.

Aligned with an international task force(26) and GRAPPA-OMERACT group recommendations(13), the use of DAPSA + PsAID or MDA + PsAID was proposed for peripheral PsA patients' follow-up. However, DAPSA + PsAID were prioritized over MDA + PsAID. Research shows DAPSA is a disease-specific, validated and feasible tool for PsA assessment(20,27). Its main advantage compared to other composite indexes assessing 28-joints, is that DAPSA covers a greater number of joints (n=68), including some of those commonly affected in PsA patients that are not covered by DAS28(28,29). However, due to the lower time requirements, the DAS28 is still widely used in clinical practice. In addition, the main disadvantage of DAPSA is its lack of skin assessment capacity. Therefore, the GRAPPA-OMERACT group recommends undertaking skin-disease evaluation in conjunction with DAPSA measurement(13). The HCPs discussion groups proposed the combination of DAPSA + PsAID. One of the main limitations of the most composite indexes (including DAPSA) is that they do not address objective indicators of skin disease, dactylitis and enthesitis. However, HCPs proposed that these domains could be indirectly assessed via the skin and functional ability items contained in the PsAID, which is supported by the differences observed in these items between treatment responders and non-responders(30). Moreover, in Spain most patients with PsA are followed by both rheumatologists and dermatologists. Thus, the extent of skin involvement is usually considered when selecting the more appropriate therapy for the patient.

It is worth noting the importance of monitoring axial symptoms, which usually overlap with peripheral joint affectation. Although axial involvement is less frequent in patients with PsA (12%)(7,31), they are more likely to have severe psoriasis, higher tender joint counts, and worse physical function and HRQoL(31). Currently, PsA-specific composite indexes are not available and non-specific PsA instruments have been proposed to follow-up axial involvement. ASDAS has been proposed to evaluate axial PsA, whereas the GRAPPA-OMERACT group does

differentiate instruments for each type of disease(13,26). HCPs recommend the use of ASDAS (plus PsAID) in those patients with prevalent axial involvement since it includes objective and subjective measures(32,33).

By combining PROs with clinical outcomes, patients' disease perception is taken into account, thus providing patient-centered care and complementing clinical practices(34). EULAR and GRAPPA-OMERACT groups recommend the use of PROs, which is in line with the American and European drug agencies, for which data related to HRQoL are mandatory for submissions(35–37). The MERECES group unanimously agreed on the use of PsAID to assess treatment effects on patient's HRQoL. PsAID has been developed considering the patient's perspective, covering nearly all core domains, and has been tested in both clinical trials and real-world settings(21,38,39). In addition, individual PsAID items have correlated strongly with other specific PROMs, such as the skin item included in DLQI(39), supporting PsAID ability to assess skin affectation. Recently, the GRAPPA-OMERACT group has described PsAID as one of the instruments demonstrating superior measurement properties(14).

One of the main factors limiting the combined use of clinical outcomes and PROMs in routine clinical practice is the time required to complete them, by both physicians and patients. During the discussion groups, patients showed willingness to complete PROMs, even at every check-up, if they did not exceed 15 items (approximately 5-10 min). Similar results were observed in a previous study in which 115 physicians considered it reasonable to fill in a questionnaire on clinical outcomes requiring less than 5-10 minutes(13). Time of ASDAS/DAPSA + PsAID completion is in line with these preferences and with the time per consultation employed in Spain (approximately 30 and 15 minutes for the first and subsequent visits, respectively).

Current recommendations on PsA patient management state that the conceptual treatment goal should be remission or low disease activity(13,25,40). However, the specific criteria to define them is under debate(41,42). Although to establish the therapeutic objective of PsA treatment falls outside the scope of this study, our results provide useful information on which health outcomes should be considered as acceptable for continuing treatment. As the disease progresses, such health outcomes may vary and, therefore, the MERECES group has defined health outcomes for three different patient profiles with increasing levels of severity.

The recommendations provided in this document should be used as an aid to determine bDMARDs effectiveness in patients with PsA. However, decisions should also consider the patient's individual characteristics, values and preferences, and any further appraisals or possible complications of the disease or treatment.

The main strength of this study is the large number of highly experienced experts from different Spanish regions who participated in the Delphi consultation. In addition, we followed rigorous research methods, with both patient and HCP representation in discussion groups.

This study has some limitations to take into consideration. HCPs were mostly rheumatologists, which may have biased results towards the greater preference for DAPSA (without objective skin assessment) compared to MDA (with objective skin assessment). However, it is important to note that DAPSA feasibility was one the main reasons for its preference in routine clinical practice. In addition, this consensus has been contextualized within the Spanish health system, which may differ in other countries. Nonetheless, in general terms, the recommendations established in this study are in line with other international approaches (e.g. GRAPPA-OMERACT).

As far as we know, this is the first multi-disciplinary consensus on the evaluation of bDMARDs effectiveness in PsA, in routine clinical practice. A combination of clinical outcome measures and PROMs has been agreed upon to establish the minimum health outcomes for treatment continuation. The consensus reached may help in making decisions about the continuity of biological therapy, in a standardized manner through appropriate outcome measures.

REFERENCES

1.   Anandarajah AP, Ritchlin CT. The diagnosis and treatment of early psoriatic arthritis. Nat Rev Rheumatol 2009;5:634-41.

2.   Kawalec PP, Malinowski KP. The indirect costs of psoriatic arthritis: systematic review and meta-analysis. Expert Rev Pharmacoecon Outcomes Res 2015;15:125-32.

3.   Kennedy M, Papneja A, Thavaneswaran A, Chandran V, Gladman DD. ACR Meeting. Arthritis Rheum 2012;64:S1-1216.

4.   Armstrong AW, Schupp C, Wu J, Bebo B. Quality of Life and Work Productivity Impairment among Psoriasis Patients: Findings from the National Psoriasis Foundation Survey Data 2003-2011. PLoS One 2012;7:0-5.

5.   Tillett W, Shaddick G, Askari A, Cooper A, Creamer P, Clunie G, et al. Factors influencing work disability in psoriatic arthritis: first results from a large UK multicentre study. Rheumatology 2015;54:157-62.

6.   Helliwell P, Coates L, Chandran V, Gladman D, de Wit M, FitzGerald O, et al. Qualifying Unmet Needs and Improving Standards of Care in Psoriatic Arthritis. Arthritis Care Res

(Hoboken) 2014;66:1759-66.

7.   Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis. Longo DL, editor. N Engl J Med
        2017;376:957-70.

8.   Kang EJ, Kavanaugh A. Psoriatic arthritis: latest treatments and their place in therapy.
        Ther Adv Chronic Dis 2015;6:194-203.

9.   Mahmood F, Coates LC, Helliwell PS. Current concepts and unmet needs in psoriatic
        arthritis. Clin Rheumatol 2018;37:297-305.

10.   Orbai A-M, de Wit M, Mease P, Shea JA, Gossec L, Leung YY, et al. International patient
        and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Ann
        Rheum Dis 2017;76:673-80.

11.   Lavallee DC, Chenok KE, Love RM, Petersen C, Holve E, Segal CD, et al. Incorporating
        Patient-Reported Outcomes Into Health Care To Engage Patients And Enhance Care.
        Health Aff 2016;35:575-82.

12.   Gladman DD, Mease PJ, Strand V, Healy P, Helliwell PS, Fitzgerald O, et al. Consensus on
        a core set of domains for psoriatic arthritis. J Rheumatol 2007;34:1167-70.

13.   Coates LC, FitzGerald O, Merola JF, Smolen J, van Mens LJJ, Bertheussen H, et al. Group
        for Research and Assessment of Psoriasis and Psoriatic Arthritis/Outcome Measures in
        Rheumatology Consensus-Based Recommendations and Research Agenda for Use of
        Composite Measures and Treatment Targets in Psoriatic Arthritis. Arthritis Rheumatol
        2018;70:345-55.

14.   Højgaard P, Klokker L, Orbai A-M, Holmsted K, Bartels EM, Leung YY, et al. A systematic
        review of measurement properties of patient reported outcome measures in psoriatic
        arthritis: A GRAPPA-OMERACT initiative. Semin Arthritis Rheum 2018;47:654-65.

15.   Palominos PE, Gaujoux-Viala C, Fautrel B, Dougados M, Gossec L. Clinical outcomes in
        psoriatic arthritis: A systematic literature review. Arthritis Care Res (Hoboken)
        2012;64:397-406.

16.   Kalyoncu U, Ogdie A, Campbell W, Bingham CO, de Wit M, Gladman DD, et al.
        Systematic literature review of domains assessed in psoriatic arthritis to inform the
        update of the psoriatic arthritis core domain set. RMD Open 2016;2:e000217.

17.   Diamond IR, Grant RC, Feldman BM, Pencharz PB, Ling SC, Moore AM, et al. Defining

consensus: A systematic review recommends methodologic criteria for reporting of Delphi studies. J Clin Epidemiol 2014;67:401-9.

18. Hohmann E, Cote MP, Brand JC. Research Pearls: Expert Consensus Based Evidence Using the Delphi Method. Arthroscopy 2018;34:3278-82.

19. Akins RB, Tolson H, Cole BR. Stability of response characteristics of a Delphi panel: application of bootstrap data expansion. BMC Med Res Methodol 2005;5:37.

20. Aletaha D, Alasti F, Smolen J. Disease activity states of the DAPSA, a psoriatic arthritis specific instrument, are valid against functional status and structural progression. Ann Rheum Dis 2017;76:418-21.

21. Gossec L, de Wit M, Kiltz U, Braun J, Kalyoncu U, Scrivo R, et al. A patient-derived and patient-reported outcome measure for assessing psoriatic arthritis: elaboration and preliminary validation of the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, a 13-country EULAR initiative. Ann Rheum Dis 2014;73:1012-9.

22. Day MS, Nam D, Goodman S, Su EP, Figgie M. Psoriatic Arthritis. J Am Acad Orthop Surg 2012;20:28-37.

23. Ogdie A, Weiss P. The Epidemiology Psoriatic Arthritis. Rheum Dis Clin North Am 2015;41:545-68.

24. D'Angiolella LS, Cortesi PA, Lafranconi A, Micale M, Mangano S, Cesana G, et al. Cost and Cost Effectiveness of Treatments for Psoriatic Arthritis: A Systematic Literature Review. Pharmacoeconomics 2018;36:567-89.

25. Torre Alonso JC, Díaz del Campo Fontecha P, Almodóvar R, Cañete JD, Montilla Morales C, Moreno M, et al. Recomendaciones de la Sociedad Española de Reumatología sobre el tratamiento y uso de terapias sistémicas biológicas y no biológicas en artritis psoriásica. Reumatol Clínica 2018;14:254-68.

26. Smolen JS, Schöls M, Braun J, Dougados M, Gerald OF, Gladman DD, et al. Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. Ann Rheum Dis 2018;77:3-17.

27. Schoels MM, Aletaha D, Alasti F, Smolen JS. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Ann Rheum Dis

2016;75:811-8.

28.   Wong PCH, Leung Y-Y, Li EK, Tam L-S. Measuring Disease Activity in Psoriatic Arthritis. Int J Rheumatol 2012;2012:1-10.

29.   Gladman DD. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64:ii14-7.

30.   Queiro R, Cañete JD, Montilla C, Abad M, Montoro M, Gómez S, et al. Minimal disease activity and impact of disease in psoriatic arthritis: a Spanish cross-sectional multicenter study. Arthritis Res Ther 2017;19:72.

31.   Mease PJ, Palmer JB, Liu M, Kavanaugh A, Pandurengan R, Ritchlin CT, et al. Influence of Axial Involvement on Clinical Characteristics of Psoriatic Arthritis: Analysis from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry. J Rheumatol 2018;45:1389-96.

32.   Kılıç G, Kılıç E, Nas K, Karkucak M, Çapkın E, Dağlı AZ, et al. Comparison of ASDAS and BASDAI as a measure of disease activity in axial psoriatic arthritis. Clin Rheumatol 2015;34:515-21.

33.   Gallino Yanzi J, Schneeberger E, Cerda O, Zaffarana C, Landi M, Rosemffet M, et al. Validation of the composite index DAPSA (Disease Activity for Psoriatic Arthritis) in a cohort of patients with psoriasis arthritis in Argentina and determination of their cut-off values. Rev argent Reum 2016;37:23-9.

34.   Weldring T, Smith SMS. Article Commentary: Patient-Reported Outcomes (PROs) and Patient-Reported Outcome Measures (PROMs). Heal Serv Insights 2013;6:HSI.S11093.

35.   FDA. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Guidance 2009.

36.   European Medicines Agency (EMA). Reflection paper on the regulatory guidance for the use of healthrelated quality of life (HRQL) measures in the evaluation of medicinal Products [Internet]. EMEA/CHMP 2005. p. 5. Available from: https://www.ema.europa.eu/documents/scientific-guideline/reflection-paper-regulatory-guidance-use-healthrelated-quality-life-hrql-measures-evaluation_en.pdf

37.   Gossec L, Smolen JS. Treatment of psoriatic arthritis: management recommendations. Clin Exp Rheumatol 2014;33:73-7.

38.   Di Carlo M, Becciolini A, Lato V, Crotti C, Favalli EG, Salaffi F. The 12-item Psoriatic

Arthritis Impact of Disease Questionnaire: Construct Validity, Reliability, and Interpretability in a Clinical Setting. J Rheumatol 2017;44:279-85.

39. Holland R, Tillett W, Korendowych E, Cavill C, Waldron N, Brooke M, et al. Validation of the Psoriatic Arthritis Impact of Disease (PsAID) Questionnaire and its potential as a single-item outcome measure in clinical practice. Ann Rheum Dis 2018;77:343-7.

40. Gossec L, Smolen JS, Ramiro S, de Wit M, Cutolo M, Dougados M, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 2016;75:499-510.

41. Mease PJ, Coates LC. Considerations for the definition of remission criteria in psoriatic arthritis. Semin Arthritis Rheum 2018;47:786-96.

42. van Mens LJJ, van de Sande MGH, van Kuijk AWR, Baeten D, Coates LC. Ideal target for psoriatic arthritis? Comparison of remission and low disease activity states in a real-life cohort. Ann Rheum Dis 2018;77:251-7.

Figure 1. Study design.

PROs, Patient Reported Outcomes. **HCPs**, Healthcare professionals.

APPENDIX

In addition to the authors, the additional investigators of MERECES Working Group participated in the consensus: Isabel Belinchón, Eugenio Chamizo, Jesús Babio, Raquel Almodóvar, Tamara del Río , José Luis Poveda, Ángel Abad, Carlos Mur, Pablo de la Cueva, Cristina Fernández-Carballido, Beatriz Joven, José A. Pinto, Ana Lozano, Leticia León, José Soto, Eva Galíndez, Mari L. García-Vivar, Ana Ruibal, Natalia Palmou, Raúl Veroz, Esteban Rubio, José L. Álvarez-Vega, Elena Alonso, Jesús Marzo, Laura Garrido, Lola Fabregas, Álvaro García-Martos, María C. Ortega, Consuelo Díaz, Juan C. Nieto, Carmen Torres, Pepe Pérez-Venegas, Jesús Sanz, Pedro Zarco, Santiago Muñoz, Txaro García-Vicuña, Carlos García-Porrúa, Francisco J. Meceiras, Carolina Álvarez-Castro, José A. Hernández-Beriain, Beatriz González, Mireia Moreno, Agustí Sellas, Julio Ramírez, Ana Urruticoechea, Andrés Ponce, Carlos Feced, Angels Martínez-Ferrer, Nagore Fernández-Llanio, Anna Martínez-Cristóbal, Cristina Campos, Arantxa Conesa, Enrique Batlle, Francisca Sivera, Vega Jovaní, Enrique Judez, Manuel Moreno, Fernando Rodríguez-Martínez, Ana María Laiz, Lourdes Mateo, Manel Pujol, Juan C. Torre, Pablo Coto, Jaume Notario, Mercé García-Font, Antonio J. Chaves, Conrad Pujol, Lluis Puig, Esteban Daudén, José L. Sánchez-Carazo, Gregorio Carretero, José L. López-Estebaranz, Anna López-Ferrer, Juan Pereyra, Lourdes Rodríguez- Fernández, José M. Carrascosa, Pedro Herranz, Ricardo Ruiz-Villaverde, Ana Turrión, Andrea M. Cuervo, Carlos A. Montilla, Concepción Delgado , Deseada Palma, José F. García-Llorente, José L. Rosales, José M. Senabre, Juan J. Lerma, María J. Moreno, María López-Lasanta, María R. Oliva , María T. Navío, Patricia Tejón, Santos Castañeda, Sara Alonso-Castro, Senen González-Suárez, Vicente Torrente, Rosa García-Portales, Jorge Cancio, Victoria Navarro , Julio A. Medina, Sergio Rodríguez-Montero, Pilar Ahijado, Azucena Hernández, Cruz Fernández-Espartero, José Antonio Mosquera, Delia Reina, Antonio García, Alejandra López, Ana Uceda and Joaquín Belzunegui.

Table 1. Sociodemographic and clinical characteristics of patients.

Characteristics	Percentage of patients
Age range	
18-35 years	20%
36-50 years	33%
51-65 years	33%
>65 years	13%
Gender, female	53%
Experienced manifestations	
Peripheral involvement	93%
Axial involvement	26%
Enthesitis	53%
Psoriasis	60%
Time from diagnosis	
< 1 year	13%
1-4 years	13%
≥ 5 years	73%
Current or previous biological agent	73%
Time from biologic treatment onset	
< 1 year	18%
1-4 years	18%
≥ 5 years	64%

Table 2. Sociodemographic characteristics of panelists

|	
Age (years), mean (SD)	48 (8.3)
Male, n (%)	60 (52.2)
Specialty, n (%)	
Rheumatologists	87 (75.7)
Dermatologists	18 (15.7)
Others	10 (8.6)
Experience (years), mean (SD)	21.7 (19.3)
Patients attended per month, mean (SD) *	311.6 (136.5)
Percentage of patients with PsA, mean (SD) *	22.7 (20.9)
Membership in multidisciplinary PsA monograph working group, n (%) *	51 (44.3)

SD, standard deviation. PsA, Psoriatic Arthritis.*Only rheumatologists and dermatologists*

Table 3. *Minimum health outcomes for treatment continuation.*

Disease activity (Composite index)	HRQoL (PROM)	Rate of agreement on treatment continuation (n=97)‡		
		Profile A[†]	Profile B[†]	Profile C[†]
Remission	Optimal	**100% ***	**100% ***	**100% ***
Remission	Suboptimal with CII	**99.0% ***	**99.0% ***	**99,0% ***
Remission	Suboptimal without CII	61.9%	**78.4% ***	**88,7% ***
Low activity	Optimal	**95.9% ***	**97.9% ***	**97,9% ***
Low activity	Suboptimal with CII	**89.7% ***	**95.9% ***	**97,9% ***
Low activity	Suboptimal without CII	25.8%	47.4%	**75,3% ***
Moderate/high activity with CII	Optimal	61.9%	67.0%	**82,5% ***
Moderate/high activity with CII	Suboptimal with CII	40.2%	51.5%	72,2%
Moderate/high activity with CII	Suboptimal without CII	7.2%	10.3%	29,9%
Moderate/high activity without CII	Optimal	10.3%	15.5%	27,8%
Moderate/high activity without CII	Suboptimal with CII	6.2%	8.2%	10,3%
Moderate/high activity without CII	Suboptimal without CII	3.1%	3.1%	2,1%

HRQoL, Health-related Quality of Life. PROM, Patient Reported Outcome Measures. CII, Clinically Important Difference.

[†] Patient profile A, Naïve to biological treatment; Patient profile B, Without structural damage and/or functional disability and/or mild-moderate psoriasis and failure to one biological treatment; Patient profile C, With structural damage, serious sequelae and failure to several biological treatments. ‡ Nine participants failed in the test scenario and their responses were subtracted from the analysis as explained in Methods section. ***** Consensus reached (≥75%).
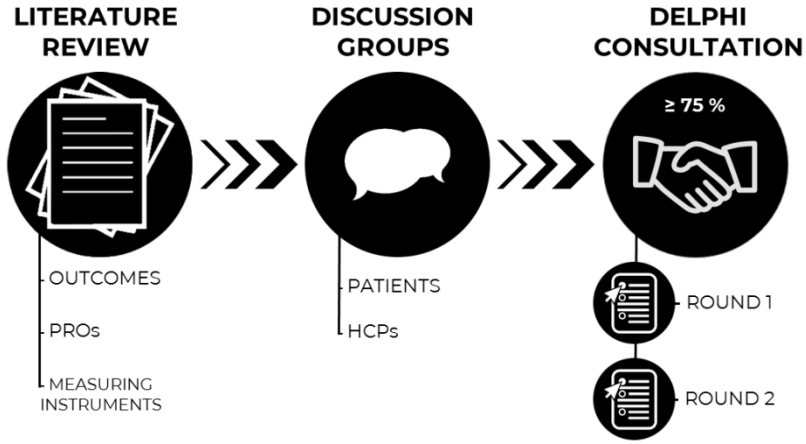
Study design / PROs, Patient Reported Outcomes. HCPs, Healthcare professionals

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