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Editorial

Treatment Continuation Guidance in Psoriatic Arthritis Clinical Care

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Psoriatic arthritis (PsA) has many disease manifestations leading to diverse patient phenotypes. Treatment responses in the same individual may diverge for concomitantly active PsA components. For this reason, evaluation of disease activity and treatment effectiveness for PsA should ideally include assessment of the complete spectrum of manifestations: psoriasis of skin and nails, arthritis, enthesitis, dactylitis, axial spondyloarthritis (SpA), systemic inflammation, and effect on life. Signs of active disease could then be systematically addressed for each individual.

Comprehensive PsA assessment is often challenging in clinical practice because of limitations on time and resources for rheumatology clinic visits. However, clinicians are uniformly confronted with effectiveness questions when treating PsA: Is the treatment working? Is it time to switch therapies? Which treatment should be next?

Cañete, *et al*, as described in this issue of *The Journal*[1], conducted a consensus exercise to define the effectiveness of biological disease-modifying antirheumatic drugs (bDMARD) and to support PsA treatment continuation decisions in clinical care. The study addresses a few scenarios relevant to clinicians such as disease severity or prior damage, peripheral and axial disease, and prior biologic experience. Criteria for bDMARD continuation are met in both peripheral and axial PsA if low disease activity (LDA) state and meaningful improvement [score improvement ≥ 3 in Psoriatic Arthritis Impact of Disease (PsAID)][2] have concomitantly been achieved (Table 1). The alternative continuation criteria, however, allow high or moderate disease activity in patients with severe PsA/damage/multiple biologic failures, as long as a major response to therapy and a patient acceptable symptom state in the PsAID (score ≤ 4) have concomitantly been achieved (Table 1). Because these effectiveness criteria define the lowest threshold for continuation of the treatment in the course in clinical care, they may shape PsA treatment and progression in the future. Comparing treatment strategies becomes essential to clarify best practices for clinicians.

Specifically in PsA, Coates, *et al*[3] reported expert consensus on very low disease activity (VLDA)/minimal disease activity (MDA) as the PsA treat-to-target (T2T) goal, and lack of consensus on a continuous measure of PsA disease activity. The latest international expert consensus on treatment targets in SpA established as a primary goal the status of remission for both peripheral and axial SpA, including PsA; and the LDA state as the alternate target[4]. The task force also unanimously recommended that T2T state should be maintained during the course of treatment, and when lost, treatment should be adapted[4]. The American College of Rheumatology/National Psoriasis Foundation PsA treatment guideline also endorsed a T2T approach versus a no-target approach[5]. More comprehensive remission definitions have been applied in a recent study in the Toronto PsA cohort[6]. They included the absence of inflammatory back pain and increased stringency of the psoriasis remission criterion to body surface area < 1%, in addition to all MDA criteria[6]. This definition, equivalent to absence of disease, was difficult to achieve and highlights the risk of persistent low levels of disease activity in PsA.

A comparison of the bDMARD effectiveness criteria proposed by Cañete, *et al*[1], and the T2T strategies above is illustrated in Table 1.

I review here the major proposal of the bDMARD continuation criteria versus existing T2T guidance and discuss the implications.

The proposal is relaxation of the primary treatment target to LDA instead of remission in both axial and peripheral PsA. This proposal raises the question of whether physicians would continue to strive for remission in their patients once LDA has been achieved. It is known that the patients' perspectives of

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Table 1. Summary of treatment targets proposed by Cãnete, *et al*[1].

Presence of Damage and/or Disability	No Damage, No Disability, No Mild/moderate Psoriasis		Damage and/or Disability and Multiple Failed bDMARD	
Subtype	Peripheral	Axial	Peripheral	Axial
Primary bDMARD continuation criteria	DAPSA ≤ 14 *and* ΔPsAID ≤ (−3)	ASDAS ≤ 2.1 *and* ΔPsAID ≤ (−3)	DAPSA ≤ 14	ASDAS ≤ 2.1
Primary T2T goal	DAPSA ≤ 4 MDA	ASDAS ≤ 1.3	DAPSA ≤ 4 MDA	ASDAS ≤ 1.3
Alternative bDMARD continuation criteria	DAPSA ≤ 4*	ASDAS ≤ 1.3*	ΔDAPSA ≤ (−85%) *and* PsAID ≤ 4	ΔASDAS ≤ (−1.1) *and* PsAID ≤ 4
Alternative T2T goal	DAPSA ≤ 14	ASDAS ≤ 2.1	DAPSA ≤ 14	ASDAS ≤ 2.1

*Alternative target allowed in this category if there is 1 bDMARD failure. bDMARD: biological disease-modifying antirheumatic drugs; DAPSA: Disease Activity in Psoriatic Arthritis; PsAID: Psoriatic Arthritis Impact of Disease; ASDAS: Ankylosing Spondylitis Disease Activity Score; T2T: treat to target; MDA: moderate disease activity.

remission and LDA align well with Disease Activity Index for Psoriatic Arthritis (DAPSA)[7], and therefore most patients will likely be happy with LDA. However, a benefit of more versus less stringent DAPSA thresholds has already been demonstrated on radiographic progression and disability[8]. In the Toronto PsA cohort, active joints and previously damaged joints were associated with radiographic progression[9]. These facts support the notion of striving for remission, and for no active and no damaged joints as early as possible in the disease course. Continuation of bDMARD even though T2T has not been met may lead to disease progression and damage in the long term. For this reason, these criteria should be viewed as an intermediate step in achieving T2T and not a replacement strategy.

The possibility exists of giving up on achieving remission in people with severe disease, established damage or disability, and multiple biologic failures. Specifically, for advanced or severe PsA after multiple prior bDMARD, high and moderate disease activity may be accepted if a major therapeutic response were achieved and if the patient acceptable symptom state for health-related quality of life (HRQOL) as measured by the PsAID is also achieved. One alarming aspect of this proposal is the concept of allowing high disease activity and MDA in exactly the people with PsA who are at greatest risk of damage progression: patients with accumulated damage/disability and many bDMARD failures. Fortunately, this situation would only rarely occur in clinical practice because it applies to people with PsA who have DAPSA scores above 97. In this situation the provision of an 85% DAPSA response would likely take care of the PsAID threshold with seemingly little additional value to the HRQOL criterion. We should be asking what the rationale and risk benefit profile of continuing a bDMARD is, if we cannot change the disease activity category and therefore cannot alter disease course and progression?

Regarding no dedicated psoriasis outcomes, one study analyzed T2T status in a cohort of participants with PsA who had quiescent disease according to their rheumatologist, and has been receiving stable treatment for at least 6 months[10]. In this cohort, DAPSA remission and LDA were more frequently met compared to VLDA/Psoriatic Arthritis Disease Activity Score remission and MDA, respectively. Of people in MDA in the study, which included assessment of both skin and joints, only about 50% had concordant quiescent disease in both psoriasis and arthritis, while a quarter had discrepant active psoriasis, and another quarter had discrepant active arthritis. Active psoriasis occurred in a proportion of 26% in MDA, and was comparable to DAPSA LDA, where 30% had active psoriasis using the same criterion (Psoriasis Area and Severity Index > 1). Therefore, active psoriasis may be missed in about one-third unless it is a required criterion, simply because of frequent divergence of disease activity of psoriasis and arthritis, and their course during therapy, in PsA. What this study teaches us is that psoriasis assessment should not be overlooked in deciding treatment success and may present an advantage in distinguishing therapies specific to PsA pathophysiologic pathways.

Another aspect is integration of disease activity targets with targets regarding the effect on life. The addition of a PsAID response to the low disease target is novel and welcome. It adds elements of skin involvement perception from the patient as well as functional status, fatigue, and effect on life. The single item of the PsAID assessing patient-reported skin problems cannot compensate for dedicated psoriasis assessment. The thresholds required by the bDMARD continuation criteria will need to be validated in this context. For example, in a recent international multicenter study of remission and flare in PsA[11], the magnitude of a PsAID response with change in treatment averaged 0.8 points (SD 3.4) in men and 2.1 points (SD 3.1) in women, lower than the proposed threshold of 3 points in this recommendation, and with significant variability. The disease activity–life effect combined treatment target requires validation in PsA treatment cohorts.

Continuation of bDMARD criteria may serve as an intermediate step in achieving treatment goals. Overall, they integrate well with the PsA core outcome set and are in tune with the recent provisional endorsement of the PsAID by the Group for Research and Assessment of Psoriatic Arthritis and Outcome Measures in Rheumatology[12,13] Clinical Trials and longitudinal studies (Table 2).

Points for improvement in the treatment continuation

Table 2. Parallel between the psoriatic arthritis (PsA) core outcome set (COS) and the proposed effectiveness targets.

PsA COS	Peripheral		Axial
	DAPSA	PsAID	ASDAS
Arthritis	68 tender/66 swollen joint counts	—	—
Dactylitis	—	—	—
Enthesitis	—	—	—
Spondyloarthritis	—	—	BASDAI – Duration morning stiffness
Psoriasis	—	PsAID – Psoriasis	—
Nail psoriasis	—	—	—
Pain	Pain VAS	PsAID – Pain	BASDAI – Spinal pain BASDAI – Peripheral pain
Patient global	Patient global assessment VAS	—	Patient global assessment
Physical function	—	PsAID – Functional capacity	—
Fatigue	—	PsAID – Fatigue	—
Life effect/HRQOL		PsAID total score	
Systemic inflammation	CRP	—	CRP

DAPSA: Disease Activity in Psoriatic Arthritis; PsAID: Psoriatic Arthritis Impact of Disease; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS: visual analog scale; HRQOL: health-related quality of life; CRP: C-reactive protein.

criteria are inclusion of dedicated psoriasis assessments, validation of disease activity and effect on life response thresholds in axial, peripheral, early, and advanced disease, and defining limitations on duration of time allowed outside T2T, so that treatment can be switched if T2T is not achieved in the designated 3–6 month time frame[4]. Also, there is no reason to limit these criteria to bDMARD and not apply them to other therapies as well. As specified in all treatment guidelines, any treatment decisions need integration with the patient's comorbidities, risks of adverse events, and personal choices and contexts.

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