Minimal Disease Activity and Remission in Psoriatic Arthritis Patients Treated with Anti-TNF-α Drugs

Fabio Massimo Perrotta, Antonio Marchesoni, and Ennio Lubrano

ABSTRACT. ***Objective.*** A state of remission is the target of therapy in chronic arthritis. The aim of the present study was to assess the rate of minimal disease activity (MDA) and remission in patients with psoriatic arthritis (PsA) treated with tumor necrosis factor (TNF-α) blockers. Disease characteristics and predictors of MDA were also evaluated.

Methods. Patients fulfilling the ClASsification for Psoriatic ARthritis (CASPAR) criteria and treated with TNF-α blockers adalimumab, etanercept, or golimumab were enrolled and prospectively followed every 4 months for 1 year in a clinical practice setting. Patients were considered in MDA when they met at least 5/7 of the criteria previously defined. Other remission criteria evaluated were 28-joint Disease Activity Score-C-reactive protein (DAS28-CRP) < 2.6 and Disease Activity in Psoriatic Arthritis (DAPSA) score ≤ 3.3. Patients achieving MDA were compared to non-MDA to identify outcome predictor factors.

Results. Of the 75 patients treated with TNF-α blockers, at baseline no patients were in MDA or had a DAPSA score ≤ 3.3, while 25 (21.3%) had a DAS28-CRP score < 2.6. Five patients (6%) discontinued treatment because of side effects or inefficacy during followup. After 12 months, MDA was achieved in 46 patients (61.3%). No difference was found among the 3 anti-TNF-α drugs. Predictors for MDA were found to be male sex, high CRP, high erythrocyte sedimentation rate, and low Health Assessment Questionnaire.

Conclusion. In our prospective observational study, based on a clinical practice setting, MDA was achieved in 61.3% of patients treated with TNF-α blockers, identifying this as an achievable target for patients with PsA. Predictors of remission were also identified. (First Release December 15 2015; J Rheumatol 2016;43:350–5; doi:10.3899/jrheum.150805)

Key Indexing Terms:
PSORIATIC ARTHRITIS — MINIMAL DISEASE ACTIVITY
REMISSION — ANTI–TUMOR NECROSIS FACTOR

Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with psoriasis with a prevalence of 0.02–0.42%[1] in the general population and 13.8–30% among patients with psoriasis[1,2]. The peripheral joint involvement of PsA is progressive in the majority of patients, reinforcing the need for optimal management and treatment strategies[3]. Moreover, patients with PsA have functional impairment, reduced quality of life, and a significant increase in early mortality compared to the general population[4]. In the context of this multifaceted disease, the concept of remission is still considered an unmet need[5]. Treatment with tumor necrosis factor-α (TNF–α) blockers showed to be effective in clinical trials and in real life, with a reduction in disease activity variables and radiographic progression[6,7]. But the real effect of anti-TNF–α therapy in controlling all the different clinical features of PsA such as dactylitis, enthesitis, and axial involvement is still unclear.

In patients with PsA, as well as in rheumatoid arthritis (RA), a state of remission or low disease activity is the target of therapy. In this context, the definition of clinical response or remission has to consider all disease domains. In 2010, Coates, *et al* developed a composite outcome measure as a target of treatment for patients with PsA that encompasses most of the disease domains[8]. Patients are considered in minimal disease activity (MDA) when they meet 5/7 of the following criteria: tender joint count ≤ 1; swollen joint count (SJC) ≤ 1; Psoriasis Activity and Severity Index (PASI) ≤ 1 or body surface area ≤ 3; patient pain visual analog scale (VAS) score of ≤ 15; patient global disease activity VAS score of ≤ 20; Health Assessment Questionnaire (HAQ) score ≤ 0.5; and tender entheseal points ≤ 1. These criteria were validated using interventional trial data[9]. Achieving sustained

From the Academic Rheumatology Unit, Department of Medicine and Health Science Vincenzo Tiberio, University of Molise, Campobasso; Rheumatology Unit, Orthopedic Institute G. Pini, Milan, Italy.

F.M. Perrotta, MD, PhD, fellow in Translational and Clinical Medicine, Academic Rheumatology Unit, Department of Medicine and Health Science Vincenzo Tiberio, University of Molise; A. Marchesoni, MD, Consultant Rheumatologist, Rheumatology Unit, Orthopedic Institute G. Pini; E. Lubrano, MD, PhD, Aggregate Professor of Rheumatology and Consultant Rheumatologist, Academic Rheumatology Unit, Department of Medicine and Health Science Vincenzo Tiberio, University of Molise.

Address correspondence to Dr. E. Lubrano, Dipartimento di Medicina e di Scienze per la Salute Vincenzo Tiberio, Università del Molise, Via Giovanni Paolo II, C/da Tappino, 86100 Campobasso, Italy. E-mail: enniolubrano@hotmail.com

Accepted for publication October 16, 2015.

MDA (defined as MDA for over 12 months at consecutive clinic visits) was found to reduce radiographic joint damage progression over a 3-year period, with an increase in damaged joint count of 0.9 in patients persistently in MDA compared to an increase of 2.4 in those not achieving sustained MDA[10]. In a recent study involving 306 patients of a retrospective cohort, Haddad, *et al* found that MDA was achieved in 64% of patients, and predictors of MDA were normal erythrocyte sedimentation rate (ESR) and male sex[11].

The complexity of disease led to the development of a number of other disease activity measures and definitions of remission such as the Disease Activity Index for Psoriatic Arthritis (DAPSA), the Composite Psoriatic Disease Activity Index (CPDAI), and the Psoriatic Arthritis Disease Activity Score (PASDAS), which were used in clinical trials and in real-life experiences[12,13]. The aim of our study was to identify MDA at 12 months in patients with PsA taking TNF-α blocker therapy and to describe the disease characteristics of patients who achieve MDA. Secondary targets were to compare MDA status with the indices of disease activity and to identify predictors for MDA.

MATERIALS AND METHODS

Patients were enrolled at the Rheumatology Unit, Department of Medicine and Health Science, University of Molise. All patients fulfilled the ClASsification for Psoriatic ARthritis (CASPAR) criteria[14]. TNF-α blockers were prescribed according to the Group of Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommendations[15]. Each subject's written consent was obtained according to the Declaration of Helsinki, and the study was approved by the local ethics committee.

Patient selection. All the patients with PsA who were taking adalimumab (ADA; 40 mg every other week), etanercept (ETA; 25 mg twice/weekly or 50 mg/weekly), or golimumab (GOL; 50 mg/monthly) from October 2012 to September 2014 were considered potentially eligible for the study. Exclusion criteria were (1) age < 18 years; (2) treatment with anti-TNF-α during the 30 days before baseline visit, and (3) MDA state before the initiation of TNF-α blocker therapy or at the baseline visit. The enrolled patients were evaluated at baseline (T0) before starting anti-TNF-α and followed prospectively every 4 months for 1 year according to clinical practice. The choice of a specific agent was based on the preference of patients and physicians.

Data collection. Patient data collection included a detailed history, physical examination, record of current use of medications, and laboratory assessment. Demographics and baseline disease characteristics comprised age, sex, age at diagnosis of psoriasis and PsA, disease duration, and pattern of articular manifestation. The definition of axial disease was based on the presence of clinical (spinal inflammatory pain according to the Calin criteria) and/or radiological axial involvement[16]. For the definition of the pattern of peripheral joint involvement, both history and current manifestations were used. The clinical assessment documented the patient's functional class, number of tender joints (of the 68 assessed joints), SJC (total of 66 joints), enthesitis, and dactylitis. Enthesitis was measured using the Maastricht Ankylosing Spondylitis Enthesitis Score[17], and dactylitis as present/absent. Skin assessment included the PASI score and the body surface area[18]. Patients also completed self-reported questionnaires including the Health Assessment Questionnaire (HAQ)[19] and a patient's global assessment (PtGA) and pain assessment on the visual analogic scale (VAS)[20]. Physician's global evaluation of disease on VAS was also recorded. Laboratory investigations included ESR and C-reactive protein (CRP).

Response criteria. MDA was identified according to Coates, *et al*[8] and assessed at 4, 8, and 12 months after the start of anti-TNF-α therapy. DAPSA score was identified according to Nell-Duxneuner, *et al*[13]. DAPSA score and DAS28-CRP[21] were also assessed at each visit. DAPSA was calculated by adding the number of tender and swollen joints, VAS pain, PtGA, and CRP (mg/dl). A DAPSA score ≤ 3.3 defined remission according to Husic, *et al*[22]. DAS28-CRP < 2.6 identified remission[23].

Statistical analysis. Categorical variables were analyzed by chi-squared test with Yates' correction or Fisher's exact test. The significance of the differences was determined using the Mann–Whitney U test for unpaired samples and the Wilcoxon test for paired samples. The probability of achieving MDA was explored using OR (lower and upper 95% CI) of outcome relative to the main variables. OR was interpreted as 1.5 to 1 weak association, 2.5 to 1 moderate association, 4 to 1 strong association, and 10 to 1 very strong association. Multivariate analysis was also performed. Correlations among the different variables were assessed using Spearman test for nonparametric variables. Concordance was assessed using Cohen's κ. The results were expressed as median (25th–75th percentile). P values < 0.05 were considered significant.

RESULTS

At baseline, 75 patients were enrolled and treated with TNF-α blockers. Methotrexate, sulfasalazine, leflunomide, and cyclosporine were used, respectively, in 67 (89.3%), 36 (48%), 10 (13.3%), and 19 (25.3%) patients. No patients were in MDA or had a DAPSA score ≤ 3.3 at baseline, while 25 (21.3%) had a DAS28-CRP score < 2.6. Table 1 shows the demographic and clinical characteristics of the study population. No differences were found between males and females. Five patients (6%) discontinued treatment because of side effects or inefficacy during followup. After 12 months, MDA was achieved in 46 (61.3%) of the 75 patients with PsA. Figure 1 shows MDA, DAS28-CRP remission, and DAPSA remission at baseline, 4 (T4), 8 (T8), and 12 (T12) months. At T12, DAPSA and DAS28 remission was achieved, respectively, in 36% and 69.3% of patients. The percentage of patients achieving MDA, DAPSA remission and DAS28 remission increased significantly from baseline to T12. Moreover, the percentage of patients achieving DAPSA remission was significantly lower than the percentage of patients achieving DAS28-CRP remission criteria ($p < 0.001$) or MDA ($p < 0.01$). No statistical differences were found among the 3 anti-TNF-α in relation to the index used to define remission, but the study was underpowered to detect differences. MDA rates for the 3 drugs at the various timepoints are depicted in Figure 2.

The association of MDA with the main variables was studied. For this purpose, the values categorized were age (≤ or > 40 yrs), disease duration (≤ or > 2 yrs), CRP (low ≤ 0.5, high > 0.5 mg/dl), ESR (low ≤ 15, high > 15 mm/h), and HAQ (low ≤ 0.5, high > 0.5). Table 2 shows the OR (95% CI) of achieving MDA at Month 12 according to the baseline values of the studied variables, by univariate and/or multivariate analysis. Independent predictors of MDA were male sex (2.67/1.21–5.90; p = 0.01), high CRP (3/1.07–8.38; p = 0.04), high ESR (3.32/1.61–5.98; p = 0.03), absence of axial involvement (4.26/1.42–12.7; p = 0.01), and low HAQ score (9.56/2.11–43.24; p < 0.01). Table 3 shows the concordance between the 3 indices in defining remission. Overall, the

Table 1. The main demographic and clinical features of the study population (75 patients with PsA treated with TNF-α blockers). Results are expressed as median/25th–75th percentile unless otherwise indicated.

Variables	
Male/female	35/40
Age, yrs	52/46.75–62
Disease duration, yrs	6.5/3–12
Articular manifestations (%)	
Axial	50.6
Peripheral arthritis	91.9
Enthesitis	41.4
Dactylitis	22.6
Extraarticular manifestations (%)	
Uveitis	5.6
IBD	1.3
DAS28-CRP*	3.71/2.7–5.06
DAPSA	20.6/13.6–29.6
Tender joint	5/2–12
Swollen joint	2/0–7
ESR, mm/h	23/12.75–29
CRP, mg/dl	0.8/0.39–1.2
PtGA	52/40–65
VAS pain	52.5/40–65
VAS physician	45/35–50
HAQ	0.75/0.62–1.25
PASI	1.3/0–2.05
MASES	1/0–2
Concomitant treatment at baseline (%)	
DMARD	49 (39.5)
Prednisone intake	39 (31.5)
NSAID intake	99 (79.8)
Anti–TNF-α therapy (%)	
ADA	39 (31.4)
ETA	62 (50)
GOL	23 (18.5)

PsA: psoriatic arthritis; TNF: tumor necrosis factor; IBD: inflammatory bowel disease; DAS28: 28-joint Disease Activity Score; DAPSA: Disease Activity Index for Psoriatic Arthritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PtGA: patient's global assessment; VAS: visual analog scale; HAQ: Health Assessment Questionnaire; PASI: Psoriasis Area and Severity Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; DMARD: disease-modifying antirheumatic drugs; NSAID: non-steroidal antiinflammatory drugs; ADA: adalimumab; ETA: etanercept; GOL: golimumab.

concordance was poor at all timepoints, with the exception of the concordance between DAPSA score and MDA at 4 and 12 months, which was moderate.

DISCUSSION

Remission or low disease activity status is the goal of therapy in chronic inflammatory arthritis. In RA, using DAS28 or American College of Rheumatology criteria, remission was achieved in about one-third of patients, especially in early disease[24]. In axial spondyloarthritis (axSpA) treated with anti-TNF-α, remission was achieved in 53.2% of the patients with the nonradiographic form and in 50.9% of the patients with ankylosing spondylitis (AS), in a clinical practice setting[25,26].

In our study, 61.3% of the patients with PsA treated with ETA, ADA, or GOL were in MDA after 12 months of treatment. In the ADEPT trial, it was demonstrated that MDA could be reached in 33.8% of patients after 24 weeks of ADA treatment[27], while in the IMPACT1 and IMPACT2 trials, MDA was reached in 48% and 52% of patients after 16 and 24 weeks of treatment, respectively, with infliximab[9]. Our real-life data showed a similar response rate, but with an increase in the number of patients who reached MDA at 12 months. In a recent report, Haddad, *et al* demonstrated a very similar rate of MDA (64%) in a cohort of patients with PsA treated with anti-TNF-α[11]. Other studies in a setting of clinical practice reported very similar response rates[28]. An interesting result of our work was the almost doubling in efficacy of anti-TNF in achieving remission from T4 to T8. This could be related to some components such as PtGA, VAS pain, and SJC. These were the main clinical components improved by the biologic treatment in that period of observation, as demonstrated by the increasing percentage of patients who reach VAS pain ≤ 15, PtGA ≤ 20, and SJC ≤ 1 (respectively, 117%, 64.2%, and 53.3%) at T8 increases compared to T4. The consistency of the data yielded by observational studies seems to suggest that in patients with PsA, the expected MDA rate after 12 months of anti-TNF-α therapy should be about 60–65%. The remaining 35–40% of patients not in MDA after 1 year of this therapy might either experience an early loss of efficacy or have a disease driven by cytokines other than TNF-α. In the latter case, other treatments targeted to different inflammatory pathways might prove useful.

In our study, predictors of response to treatment with TNF-α blockers were male sex, preserved functional status, high ESR, and CRP. The finding that patients with high inflammatory burden were more likely to achieve MDA when treated with anti-TNF-α is in keeping with findings in studies on patients with AS or axSpA[29,30]. However, Haddad, *et al* showed normal ESR as a predictor factor for MDA. This difference could be explained by the different characteristics of the 2 cohorts of patients and by the different design of the study: in our prospective work, 64% of patients had abnormal ESR values (defined as ESR > 20 mm/h) as opposed to 25% of patients in the study by Haddad, *et al*. In a large study including patients with early PsA from a Swedish register, a high rate of MDA (40.1%) was found after 5 years of followup. Also in that study, male sex was a predictor of MDA[31]. Although no statistical difference was found in the item of pain or PtGA between men and women, a sex-related propensity for higher pain levels cannot be excluded and may explain these results. Another association was with lower HAQ. Although HAQ might be related to damage, it is also associated with disease activity. Our results could be in contradiction, because the chance of achieving MDA is associated with higher disease activity (i.e., high CRP and ESR), but also with lower HAQ. In our study, however, HAQ

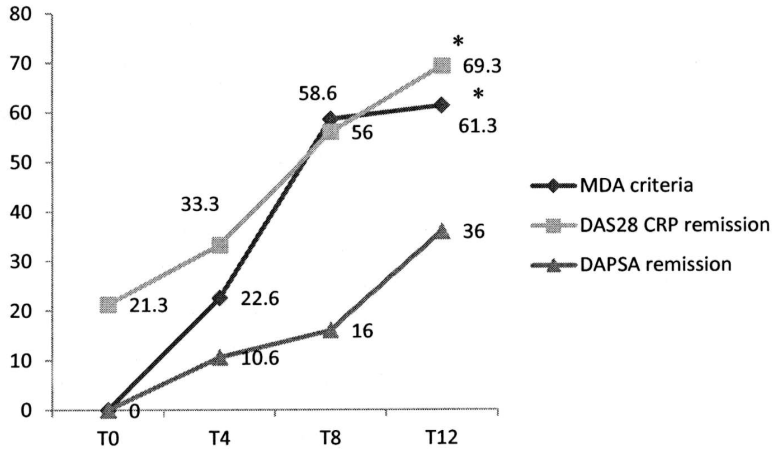

Figure 1. Remission rate according to the various criteria. * P < 0.01 vs DAPSA remission. MDA: minimal disease activity; DAS28: 28-joint Disease Activity Score; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis.

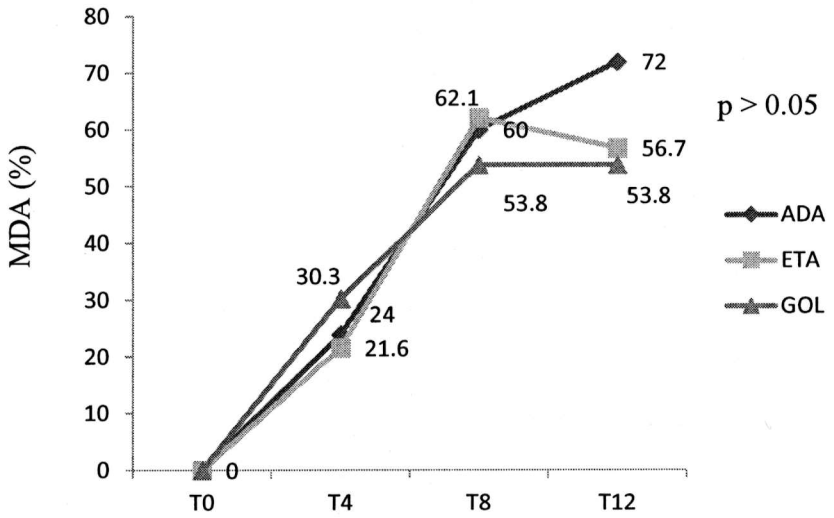

Figure 2. MDA rate in patients with PsA treated with ADA (n = 25), ETA (n = 37), and GOL (n = 13). MDA: minimal disease activity; PsA: psoriatic arthritis; ADA: adalimumab; ETA: etanercept; GOL: golimumab.

correlated well with the number of damaged joints, while a poor correlation was found between ESR and CRP. Indeed, this could be in keeping with a possible role of HAQ as a measure of severity in this group of patients.

In our work, the absence of axial involvement is associated with higher probability to reach a state of MDA. In particular, our results showed that the absence of axial involvement was associated with higher probability to reach a state of MDA. MDA, *per se*, is more influenced by peripheral joint involvement; or alternatively, the presence of axial involvement might be associated with a more severe disease. It has been suggested that MDA may not define a state of remission or near-remission. A definition of remission in PsA has not been uniformly accepted: DAPSA score ≤ 3.3 and DAS28-CRP < 2.6 could be useful surrogates of remission, especially in patients with PsA who have predominant peripheral joint involvement. In our study, the percentage of patients achieving DAS28-CRP remission criteria (69.3%) and MDA did not statistically differ, while the percentage of patients with PsA who reached DAPSA score (36%) was significantly lower (p < 0.01). It is clear that composite measures used in RA such as the DAS28 rely mainly on disease activity in 28 joints, and therefore do not fully represent the peripheral joint involvement of PsA. In fact, DAS28 is a measure tailored mainly for small joint involvement of the hands, while PsA is a real heterogeneous

Table 2. OR (95% CI) of achieving MDA at Month 12 according to the baseline variable values.

Variables	OR (95% CI), Univariate Analysis	p	OR (95% CI), Multivariate Analysis	p
Male vs female	2.67 (1.21–5.90)	0.01	2.23 (0.58–8.575)	NS
Age: ≤ 40 yrs vs > 40 yrs	2.86 (0.75–10.8)	NS	0.946 (0.88–1.00)	NS
Disease duration: ≤ 2 yrs vs > 2 yrs	1.94 (0.48–7.86)	NS	1.03 (0.13–7.87)	NS
Enthesitis: absence vs presence	0.53 (0.22–1.24)	NS	0.61 (0.34–1.14)	NS
Uveitis: absence vs presence	1.19 (0.20–6.86)	NS	1.25 (0.35–6.99)	NS
IBD: absence vs presence	1.08 (0.54–1.56)	NS	1.07 (0.55–1.60)	NS
Axial involvement absence vs presence	4.26 (1.42–12.7)	0.01	7.62 (1.38–41.9)	< 0.01
HAQ, low vs high	9.56 (2.11–43.24)	< 0.01	53.1 (3.25–869.6)	< 0.01
ESR, high vs low	3.32 (1.61–5.98)	0.03	11.9 (1.75–81.7)	0.01
CRP, high vs low	3 (1.07–8.38)	0.04	45.2 (3.64–560.6)	< 0.01
PtGA, VAS ≤ 40 vs VAS > 40	2.77 (0.95–8.1)	NS	2.32 (0.87–6.51)	NS
Pain, VAS ≤ 40 vs VAS > 40	2.77 (0.95–8.1)	NS	2.55 (0.66–9.31)	NS
DMARD, concomitant use vs anti-TNF monotherapy	0.39 (0.14–1.09)	NS	0.89 (0.77–1.23)	NS

MDA: minimal disease activity; IBD: inflammatory bowel disease; HAQ: Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PtGA: patient's global assessment: VAS: visual analog scale; DMARD: disease-modifying antirheumatic drugs; TNF: tumor necrosis factor; NS: not significant.

Table 3. Concordance (Cohen's κ) between the different response criteria. T numbers refer to months.

Criteria	T0	T4	T8	T12
MDA and DAS28-CRP remission	—	0.18	0.18	0.11
DAPSA remission and DAS28-CRP remission	—	0.30	0.13	0.15
MDA and DAPSA remission	—	0.53	0.36	0.43

MDA: minimal disease activity; DAS28: 28-joint Disease Activity Score; CRP: C-reactive protein, DAPSA: Disease Activity Index for Psoriatic Arthritis.

disease. Moreover, these composite measures do not fully evaluate the multiple clinical domains of psoriatic disease (e.g., enthesitis, dactylitis, and skin involvement). Nevertheless, another study has reported that the DAS28 is a valid instrument for measuring disease activity regarding response to biologic therapies[32]. As indicated by our study, a DAPSA score ≤ 3.3 seems to represent a more stringent definition of remission. Overall, we found a moderate concordance (k > 0.4) between MDA and DAPSA remission criteria at 4 and 12 months of treatment. This result proves that DAPSA and MDA might have an acceptable agreement, even if they are composite indices, made to a certain extent by items exploring different domains. In particular, DAPSA does not explore skin and entheseal involvement, but includes an objective variable of inflammation (CRP) and VAS pain.

A limitation of our study was the absence of PASDAS and CPDAI as response criteria. Both these criteria might prove to be well-suited to assess disease activity in PsA. However, because they are not used in our clinical practice on a regular basis, we could not include them in our study.

Despite the relatively small number of patients, our present study confirmed that a high rate of MDA may be achieved by patients with PsA treated with anti-TNF-α drugs. It also showed that MDA, DAS28, and DAPSA are not easily interchangeable measures of disease activity in PsA.

REFERENCES

1. Chandran V, Raychaudhuri SP. Geoepidemiology and environmental factors of psoriasis and psoriatic arthritis. J Autoimmun 2010;34:314-21.
2. Ibrahim G, Waxman R, Helliwell PS. The prevalence of psoriatic arthritis in people with psoriasis. Arthritis Rheum 2009;61:1373-8.
3. McHugh NJ, Balachrishnan C, Jones SM. Progression of peripheral joint disease in psoriatic arthritis: a 5-yr prospective study. Rheumatology 2003;42:778-83.
4. Gladman DD. Disability and quality of life considerations. Psoriatic arthritis. In: Gordon GB, Ruderman E, eds. Psoriasis and psoriatic arthritis: an integral approach. Heidelberg: Springer-Verlag; 2005:118-237.
5. 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 2014;66:1759-66.
6. Ash Z, Gaujoux-Viala C, Gossec L, Hensor EM, FitzGerald O, Winthrop K, et al. A systematic literature review of drug therapies for the treatment of psoriatic arthritis: current evidence and meta-analysis informing the EULAR recommendations for the management of psoriatic arthritis. Ann Rheum Dis 2012;71:319–26.
7. Glintborg B, Østergaard M, Dreyer L, Krogh NS, Tarp U, Hansen MS, et al. Treatment response, drug survival, and predictors thereof in 764 patients with psoriatic arthritis treated with anti–tumor necrosis factor α therapy: results from the nationwide Danish DANBIO registry. Arthritis Rheum 2011;63:382-90.
8. Coates LC, Fransen J, Helliwell PS. Defining disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis 2010;69:48-53.
9. Coates L, Helliwell P. Validation of minimal disease activity criteria for psoriatic arthritis using interventional trial data. Arthritis Care Res 2010;62:965-9.
10. Coates LC, Cook R, Lee KA, Chandran V, Gladman DD. Frequency, predictors, and prognosis of sustained minimal disease activity in an observational psoriatic arthritis cohort. Arthritis Care Res 2010;62:970–6.
11. Haddad A, Thavaneswaran A, Ruiz-Arruza I, Pellett F, Chandran V, Cook RJ, et al. Minimal disease activity and anti-tumor necrosis

factor therapy in psoriatic arthritis. Arthritis Care Res 2015; 67:842-7.
12. Helliwell PS, FitzGerald O, Fransen J, Gladman DD, Kreuger GG, Callis-Duffin K, et al. The development of candidate composite disease activity and responder indices for psoriatic arthritis (GRACE project). Ann Rheum Dis 2013;72:986-91.
13. Nell-Duxneuner VP, Stamm TA, Machold KP, Pflugbeil S, Aletaha D, Smolen JS. Evaluation of the appropriateness of composite disease activity measures for assessment of psoriatic arthritis. Ann Rheum Dis 2010;69:546-9.
14. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H; CASPAR Study Group. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
15. Ritchlin CT, Kavanaugh A, Gladman DD, Mease PJ, Helliwell P, Boehncke WH, et al; Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA). Treatment recommendations for psoriatic arthritis. Ann Rheum Dis 2009;68:1387-94.
16. Lubrano E, Spadaro A, Marchesoni A, Olivieri I, Scarpa R, D'Angelo S, et al. The effectiveness of a biologic agent on axial manifestations of psoriatic arthritis. A twelve months observational study in a group of patients treated with etanercept. Clin Exp Rheumatol 2011;29:80-4.
17. Heuft-Dorenbosch L, Spoorenberg A, van Tubergen A, Landewé R, van ver Tempel H, Mielants H, et al. Assessment of enthesitis in ankylosing spondylitis. Ann Rheum Dis 2003;62:127-32.
18. Chandran V, Gottlieb A, Cook RJ, Duffin KC, Garg A, Helliwell P, et al. International multicenter psoriasis and psoriatic arthritis reliability trial for the assessment of skin, joints, nails and dactylitis. Arthritis Rheum 2009;61:1235-42.
19. Ranza R, Marchesoni A, Calori G, Bianchi G, Braga M, Canazza S, et al. The Italian version of the Functional Disability Index of the Health Assessment Questionnaire. A reliable instrument for multicenter studies on rheumatoid arthritis. Clin Exp Rheumatol 1993;11:123-8.
20. Cauli A, Gladman DD, Mathieu A, Olivieri I, Porru G, Tak PP, et al. Patient global assessment in psoriatic arthritis: a multicenter GRAPPA and OMERACT study. J Rheumatol 2011;38:898-903.
21. Fransen J, van Riel PL. The Disease Activity Score and the EULAR response criteria. Clin Exp Rheumatol 2005;23:S93-9.
22. Husic R, Gretler J, Felber A, Graninger WB, Duftner C, Hermann J, et al. Disparity between ultrasound and clinical findings in psoriatic arthritis. Ann Rheum Dis 2014;73:1529-36.
23. Shammas RM, Ranganath VK, Paulus HE. Remission in rheumatoid arthritis. Curr Rheumatol Rep 2010;12:355-62.
24. Ma MH, Scott IC, Kingsley GH, Scott DL. Remission in early rheumatoid arthritis. J Rheumatol 2010;37:1444-53.
25. Lubrano E, Perrotta FM, Marchesoni A, D'Angelo S, Ramonda R, Addimanda O, et al. Remission in nonradiographic axial spondyloarthritis treated with anti-tumor necrosis factor-α drugs: an Italian multicenter study. J Rheumatol 2015;42:258-63.
26. Spadaro A, Lubrano E, Marchesoni A, D'Angelo S, Ramonda R, Addimanda O, et al. Remission in ankylosing spondylitis treated with anti-TNF-a drugs: a national multicentre study. Rheumatology 2013;52:1914-9.
27. Mease PJ, Heckaman M, Kary S, Kupper H. Application and modifications of minimal disease activity measures for patients with psoriatic arthritis treated with adalimumab: subanalyses of ADEPT. J Rheumatol 2013;40:647-52.
28. Costa L, Caso F, Ramonda R, Del Puente A, Cantarini L, Darda MA, et al. Metabolic syndrome and its relationship with the achievement of minimal disease activity state in psoriatic arthritis patients: an observational study. Immunol Res 2015;61:147-53.
29. Vastesaeger N, van der Heijde D, Inman RD, Wang Y, Deodhar A, Hsu B, et al. Predicting the outcome of ankylosing spondylitis therapy. Ann Rheum Dis 2011;70:973-81.
30. Perrotta FM, Addimanda O, Ramonda R, D'Angelo S, Lubrano E, Marchesoni A, et al. Predictive factors for partial remission according to the Ankylosing Spondylitis Assessment Study working group in patients with ankylosing spondylitis treated with anti-TNFa drugs. Reumatismo 2014;66:208-14.
31. Theander E, Husmark T, Alenius GM, Larsson PT, Teleman A, Geijer M, et al. Early psoriatic arthritis: short symptom duration, male gender and preserved physical functioning at presentation predict favourable outcome at 5-year follow-up. Results from the Swedish Early Psoriatic Arthritis Register (SwePsA). Ann Rheum Dis 2014;73:407-13.
32. Salaffi F, Ciapetti A, Carotti M, Gasparini S, Gutierrez M. Disease activity in psoriatic arthritis: comparison of the discriminative capacity and construct validity of six composite indices in a real world. Biomed Res Int 2014;2014:528105.