Recommendations of the Brazilian Society of Rheumatology

Recommendations for the management and treatment of psoriatic arthritis

Recomendações sobre diagnóstico e tratamento da artrite psoriásica

Sueli Carneiro, Valderílio Feijó Azevedo, Rubens Bonfiglioli, Roberto Ranza, Célio Roberto Gonçalves, Mauro Keiserman, Eduardo de Souza Meirelles, Marcelo de Medeiros Pinheiro, Antonio Carlos Ximenes, Wanderley Bernardo, Percival Degrava Sampaio-Barros

Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
Universidade Federal do Paraná, Curitiba, PR, Brazil
Pontifícia Universidade Católica de Campinas, Campinas, SP, Brazil
Universidade Federal de Uberlândia, Uberlândia, MG, Brazil
Divisão de Reumatologia, Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil
Hospital São Lucas, Pontifícia Universidade Católica de Porto Alegre, Porto Alegre, RS, Brazil
Unit of Reumatology, Instituto de Ortopedia e Traumatologia, FMUSP, São Paulo, SP, Brazil
Universidade Federal de São Paulo, São Paulo, SP, Brazil
Hospital Geral de Goiânia, Goiânia, GO, Brazil
Coordinator of the Projeto Diretrizes da Associação Médica Brasileira, São Paulo, SP, Brazil
President of the Commission on Spondyloarthritis of the Brazilian Society of Rheumatology (2006-2012), São Paulo, SP, Brazil

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Description of the evidence elaboration method

The members of the Comissão de Espondiloartrites da Sociedade Brasileira de Reumatologia (Commission on Spondyloarthritis of the Brazilian Society of Rheumatology, SBR) 2010-2012 took part in the Evidence Preparation Course given by the Associação Médica Brasileira (Brazilian Medical Association, AMB) in São Paulo in the first semester of 2011. The questions were finally concluded at a meeting of the Commission on Spondyloarthritis held on 15 October 2011 in Florianópolis (SC, Brazil), during the 18th Southern Cone Rheumatology Meeting and were later approved by all the coordinators of the Brazilian Spondyloarthritis Registry. The 15 clinical questions considered to be relevant were structured using the P.I.C.O. method (patient; intervention or indicator; comparison; outcome). The literature search was conducted by searching the databases MEDLINE, EMBASE, SciElo/Lilacs, and the Cochrane Library through February, 2012 (Appendix). Critical assessment of the evidence in the selected articles was performed using the Jadad score. Next, the answers to the questions included in the Recommendations were elaborated, and all the selected references exhibit the corresponding grade of recommendation and strength of scientific evidence. The references were updated through August, 2012, entered into a single file by the coordinator, and sent to the co-authors in two successive rounds for preparation of the final version.

Grades of recommendation and strength of evidence

A: Most consistent experimental and observational studies.
B: Less consistent experimental and observational studies.
C: Case reports (uncontrolled studies).
D: Opinion that is not substantiated by critical evaluation, based on consensus, physiological studies or animal models.

☆ Study with the seal of the Brazilian Society of Rheumatology.
* Corresponding author.
E-mail: pdsampaiobarros@uol.com.br (F.D. Sampaio-Barros).
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**Objective**
To establish recommendations for the management (criteria for classification and clinical assessment) and treatment of psoriatic arthritis.

**Introduction**

Skin psoriasis is a relatively frequent condition that affects 1-3% of the overall population. Psoriatic arthritis is the most common of the non-skin manifestations of psoriasis and affects 8-42% of patients. Joint condition (arthritis, enthesitis, and/or dactylitis) may be associated with significant functional limitation of affected individuals. Therefore, early diagnosis is of paramount importance in permitting the establishment of efficient therapeutic strategies. Recently, the formulation of the Classification Criteria for Psoriatic Arthritis (CASPAR) criteria\(^1(B)\) has made the characterisation of patients with psoriatic arthritis easier and more comprehensive, while the development of novel therapies has improved the efficacy of treatment. Access to information about diagnostic and therapeutic advances related to psoriatic arthritis is indispensable to achieving a better and more thorough understanding of this disease.

1. **What are the criteria on the basis of which an individual is considered to have psoriatic arthritis?**

There are several classification criteria for psoriatic arthritis; these are described below.

a) Moll & Wright criteria: psoriasis or history of psoriasis or nail disease, negative rheumatoid factor (RF), and one of the following clinical conditions: asymmetric oligoarticular arthritis; polyarticular arthritis; distal interphalangeal predominance; predominant spondylitis; mutilating arthritis.

b) Bennett criteria: psoriasis of the skin or nails, pain and edema of soft tissue, and/or reduced mobility of at least one joint in addition to six of the following items: distal interphalangeal arthritis; asymmetric arthritis; absence of subcutaneous nodules; negative RF; inflammatory synovial fluid; synovial hypertrophy on biopsy; erosive arthritis affecting small joints; sacroiliitis; syndesmophytes; paravertebral ossification.

c) Vasey & Espinoza criteria: psoriasis or history of psoriasis or nail disease and one of the following items: peripheral distal interphalangeal involvement; dactylitis; asymmetric arthritis; osteolyis, erosive arthritis; periostitis; ankylosis; central backache or stiffness; symmetric sacroiliitis.

d) Fournié criteria (score of 11 points): psoriasis (6 points), history of psoriasis (3 points), distal interphalangeal arthritis (3 points), cervical or thoracic spinal inflammation (3 points), asymmetric arthritis (1 point), pain (2 points), HLA-B16 or B17 (6 points), negative RF (4 points), erosion of distal phalanges, osteolysis, ankylosis, bone formation, or tuft erosion (5 points).

e) European Spondyloarthropathy Study Group (ESSG) criteria: inflammatory pain in the back or synovitis and psoriasis or family history of psoriasis.

f) CASPAR criteria: confirmed inflammatory joint disease (joints, spine, or entheses) and at least three of the following: current psoriasis; personal or family history of psoriasis; dactylitis; juxta-articular bone formation (hands and feet); negative RF; psoriatic nail dystrophy\(^1(B)\). The sensitivity and specificity of the CASPAR criteria are 99.7% and 99.1%, respectively\(^1(B)\).

According to the CASPAR criteria, the clinical characteristics of psoriasis patients included psoriasis in 100% of patients, psoriatic nail dystrophy in 28.5%, negative RF in 77.1%, dactylitis in 34.2%, and juxta-articular bone formation in 34.2%. The most common clinical forms of psoriasis include those with predominance of peripheral joint inflammation (81.2%) and those with polyarticular involvement (47.8%)\(^1(B)\).

In patients with psoriatic arthritis, the Bennett criteria were positive in 10.2% of the cases, while Moll & Wright’s criteria were satisfied in 30.7% of cases, ESSG’s in 43.5%, Vasey & Espinoza’s in 46.1%, Fournié’s in 79.4%, and CASPAR in 89.7%\(^1(B)\).

The predominant clinical criteria upon diagnosis of patients with psoriatic arthritis and their corresponding relative prevalence, sensitivity, and specificity were: synovitis (151%, 51%, and 100%), enthesopathy (140%, 40%, and 100%), dactylitis (120%, 20%, and 100%), family history (118%, 51%, and 67%), inflammatory lumbar pain (113%, 13%, and 100%), and alternating buttock pain (111%, 13%, and 98%)\(^1(B)\).

The domain most frequently investigated in the assessment of patients with psoriatic arthritis is the skin [Psoriasis Area Severity Index (PASI) and Physicians’ Global Assessment of Psoriasis (PGAP)], followed by the joints (number of affected joints, distal interphalangeal involvement, and the presence or absence of symmetric polyarthritis). Other clinical features taken into consideration include enthesis [presence of pain, Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)], dactylitis [number of affected fingers and Infliximab Multinational Psoriatic Arthritis Controlled Trial Index for Dactylitis (IMPACT 1)], and nail disease [Nail Psoriasis Severity Index (NAPSI)]\(^1(B)\).

**Recommendation 1**

The CASPAR classification criteria are the most widely used criteria for psoriatic arthritis.

2. **Are there correlations among skin, nail, and joint disease activity in psoriatic arthritis?**

In patients with psoriatic arthritis, skin disease antedated arthritis in 60% of cases and occurred concomitantly in the same year in 31%, while arthritis antedated skin manifestations in 9%. There was significant correlation between the degree of skin involvement (PASI) and Schober’s test. Deformed joints were associated with high PASI scores. The score for scalp involvement exhibited a positive correlation with the number of affected joints (deformities, dactylitis, and distal interphalangeal involvement). Similarly, there was a positive correlation between nail and joint effects and between nail effects and the number of affected joints\(^1(B)\).
Nail thickening with or without surface irregularities occurred in 95.7% of cases of psoriatic arthritis. Diagnosis of nail involvement using magnetic resonance imaging was more common in patients with clinical signs of nail disease. Similarly, patients with distal interphalangeal abnormalities more often exhibited clinical signs of nail disease, showing a risk that was increased by 49.2% (B).

Nail involvement occurred significantly more often in patients with psoriatic arthritis than in patients with psoriasis alone (59% greater risk), but there was no correlation between patterns of skin and nail involvement (B). The area of affected skin was four times greater in patients with psoriasis without arthritis (9.8%) than in patients with psoriatic arthritis (2.5%) (B).

Recommendation 2

There is variable correlation between the intensity of skin manifestations and joint involvement in psoriatic arthritis. Nail alterations occur more frequently in patients with psoriatic arthritis.

3. What are the comorbidities most often associated with psoriatic arthritis?

Compared to patients with psoriasis alone, patients with psoriatic arthritis exhibited 4.9% increased risk of cardiovascular disease (number needed to harm (NNH) = 20), 17.5% increased risk of hypertension (NNH: 6), 6.2% increased risk of hyperlipidaemia (NNH: 16), 5.3% increased risk of type 2 diabetes (NNH: 19), 3.5% increased risk of obesity (NNH: 32), 4.3% increased risk of respiratory disease (NNH: 24), 6.7% increased risk of gastrointestinal disease (NNH: 14), 5.7% increased risk of neurological disease (NNH: 19), 11.4% increased risk of depression or anxiety (NNH: 9), and 4.7% increased risk of cancer (NNH: 21) (B).

Patients with psoriatic arthritis exhibited 79% increased relative risk of stroke, acute myocardial infarction, and cardiovascular death, similar to patients with psoriasis without arthritis (B).

Patients with established psoriatic arthritis exhibited 22.9-49.3% increased risk of hypertension (NNH: 2-5), 2.2-5.3% increased risk of diabetes (NNH: 19-45), 7.4-8.1% increased risk of Crohn’s disease (NNH: 12-14), and 6.4-11.8% increased risk of chronic obstructive pulmonary disease (NNH: 8-15). Patients in the early stages of psoriatic arthritis exhibited 22.8-26.6% increased risk of hypertension (NNH: 4) (B). These patients also show 22.9% increased risk of metabolic syndrome (NNH: 4) (B) as well as increased risk of atherosclerosis and peripheral vascular disease (B).

Patients with psoriatic arthritis exhibited 2-17% increased risk of thyroid-stimulating hormone (TSH) levels > 3.5 μU/mL, 12-16% increased risk of antithyroid peroxidase antibody (AbTPO) levels > 100 IU/mL, and 15-20% increased risk of thyroid autoimmunity (positive antithyroglobulin antibody – AbTg+, or AbTPO+) (B).

Uni- or bilateral uveitis was found in 25% and 37.5% of patients with psoriatic arthritis, respectively, with similar distribution of the anterior and posterior forms; on average, insidious progression occurred in 19% of cases nine years after diagnosis of arthritis (B).

Recommendation 3

Psoriatic arthritis is associated with increased risk of some comorbidities, including cardiovascular diseases, type 2 diabetes, gastrointestinal, respiratory and neuropsychiatric diseases, hypothyroidism, and uveitis.

4. What is the evidence regarding the use of corticosteroids in patients with psoriatic arthritis?

Glucocorticoids may be used as adjuvant therapy in the localised forms of the disease (oligoarticular, enthesitis, dactylitis) (D). Corticosteroid (methylprednisolone) injections in doses varying from 5-80 mg can be used in cases of joint inflammation or injury, including in the interphalangeal region (44%), knees (21%), and coxofemoral joints (9.4%). The odds of achieving clinical response in three and six months were 41.6% and 51.5%, respectively. Approximately 25.5% of the joints that responded at three months exhibited relapse (B).

The use of systemic corticosteroids in patients with psoriatic arthritis has not been consistently investigated. In fact, expert opinion contraindicates the use of systemic corticoids in psoriasis, recommending that they be restricted to special situations and only used for short periods of time. Despite those considerations, systemic corticoids were prescribed to 24.4-30% of patients with psoriatic arthritis while closely monitoring the possible worsening of the skin condition (B).

Long-term use of glucocorticoids may induce resistance, for example, in cases where psoriasis is controlled by methotrexate, in addition to its association with adverse events such as development of osteoporosis, reduced glucose tolerance, and increased incidence of infections. Discontinuation of corticoids has been associated with the occurrence of pustular psoriasis (C).

Used in 24.4% of patients with psoriatic arthritis, the most frequently employed systemic corticosteroid was methylprednisolone (65.9%), followed by deflazacort (22.8%), prednisone (4.4%), betamethasone (2.3%), and dexamethasone (2.3%). The average daily dose of methylprednisolone was 4.5 ± 1.4 mg (C).

Recommendation 4

Intra-articular corticosteroids may represent a therapeutic option in cases of mono or oligoarticular joint involvement in psoriatic arthritis. Systemic use of corticosteroids is not recommended due to a lack of evidence regarding their efficacy, a risk of severe adverse events, and relapse of skin psoriasis upon discontinuation.

5. What is the evidence regarding the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with psoriatic arthritis?

Indomethacin at a dose of 50 mg/day elicited clinical response (improvement of pain, movement limitation, and stiffness) in
62% of patients with psoriatic arthritis followed up for eight weeks; its use was associated with adverse effects such as vertigo, nausea, and headache²⁴(B).

A comparison of indomethacin with diclofenac at a dose of 75 mg/day in patients with psoriatic arthritis showed a non-significant clinical response after eight weeks to both investigated drugs and no differences between them in relation to adverse events²³(B).

The anti-inflammatory agent nimesulide at doses of 200 and 400 mg/day induced the following benefits in patients with psoriatic arthritis: reduction in pain score, reduction in scores for swelling and morning stiffness, and reduced use of analgesics, without significant increase in the number of adverse events²⁵(B).

Treatment of patients with psoriatic arthritis with celecoxib at doses of 200 and 400 mg over two weeks increased the rates of clinical response measured by the American College of Rheumatology Responders Index 20% (ACR20) by 21% (number needed to treat (NNT): 5) and 11% (NNT: 9), respectively. However, there was no difference in response between patients treated with celecoxib and untreated patients after 12 weeks²⁶(A).

**Recommendation 5**

Treatment with non-steroidal anti-inflammatory drugs represents an option for short-term symptomatic treatment of psoriatic arthritis.

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### 6. What is the evidence regarding the use of the conventional drugs methotrexate, cyclosporine, leflunomide, and sulfasalazine in patients with psoriatic arthritis?

#### Methotrexate

Methotrexate at a dose of 2-5 mg every 12 hours, given in three consecutive doses per week, did not improve swelling, morning stiffness, pain, strength, or joint involvement in patients with psoriatic arthritis over 12 weeks compared to those who did not use methotrexate; however, it reduced the physician-assessed severity scores. Its use was associated with gastrointestinal disorders, stomatitis, and increased bilirubin levels²⁷(B).

After 24 months of follow-up, no difference was found in the clinical responses (≥ 40% improvement in actively inflamed joint count) of patients with psoriatic arthritis treated with 5-7.5 mg methotrexate per week and those using NSAIDs. Radiological assessment found a non-significant increase of 16% in joint damage scores in the patients treated with methotrexate²⁸(B).

Association of methotrexate with NSAIDs since the beginning of treatment or in the second trimester of a six-month period of treatment of patients with psoriatic arthritis was beneficial relative to the activity of the disease as measured by (1) swollen or stiff joint counts; (2) global assessment by patients or doctors; and (3) pain visual analogue scale (VAS); there was no difference between the two regimens²⁹(B).

A comparison of six-month treatment with methotrexate in patients with psoriatic arthritis and rheumatoid arthritis found better results in the latter. However, in the beginning of treatment, the patients with psoriatic arthritis exhibited reduction in the number of affected joints, reduction of pain (VAS), reduction in the global assessment of disease activity by both patients and doctors, improved quality of life [Modified Health Assessment Questionnaire (MHAQ) and Medical Outcomes Study 36-item Short-Form Health Survey (SF-36)]. Nevertheless, relative to the disease activity score (DAS), the number of patients with psoriatic arthritis with DAS ≥ 2.6 and ≥ 3.2 increased 17% and 29%, respectively³⁰(B).

The adverse events most frequently associated with the use of methotrexate were nausea, photosensitisation, and aphthae (leading to discontinuation) and increased liver enzyme levels (35%)³¹(B).

#### Cyclosporine

A comparison of cyclosporine (3 mg/kg/day) and methotrexate (three consecutive 2.5-mg doses every 12 hours per week) in the treatment of psoriatic arthritis showed that after 12 months both resulted in improvement in joint swelling and pain, morning stiffness, and strength and in reduced activity of disease as assessed by patients and doctors, without difference between the treatments. Methotrexate increased liver enzyme levels, while cyclosporine did not³²(B).

Compared to sulfasalazine (2 g/day) combined with symptomatic medications or symptomatic medication alone (NSAIDs, analgesics, and/or prednisolone) over six months, cyclosporine (3 mg/kg/day) induced better results relative to pain relief and reduction in the number of affected joints. There was 34% reduction of the disease activity according to the patients’ global assessment, 24% reduction according to the doctors’ assessment, and better scores on the Arthritis Impact Measurement Scale and Spondylitis Functional Index were achieved after treatment. Compared to symptomatic treatment, cyclosporine increased the number of patients who reached ACR50 and ACR70 by 22% and 24%, respectively. Adverse events included deterioration of the function, gastrointestinal and neurological disorders, and hypertension³³(A).

In patients with psoriatic arthritis and incomplete response to methotrexate, the use of cyclosporine (2.5 mg/kg/day) over 48 weeks reduced the risk of joint involvement by 36% (NNT: 3), as well as reducing PASI and the number of swollen joints. The pain score did not change significantly, but the number of adverse events (nausea, headache, paresthesia, and burning sensation) increased³⁴(B).

A comparison of adalimumab treatment (40 mg on alternate weeks), treatment with cyclosporine (2.5-3.75 mg/kg/day) and treatment with a combination of both drugs in patients with psoriatic arthritis showed that use of the combined drugs increased the response (Psoriatic Arthritis Response Criteria) by 30% compared with cyclosporine alone (NNT: 3) and that it increased the number of patients who reached ACR50 by 51% (NNT: 2). Use of the combination regimen also improved the patients’ scores on the Health Assessment Questionnaire Disability Index and reduced the use of NSAIDs and corticosteroids by 51% (NNT: 2)³⁵(B).

#### Leflunomide

Use of leflunomide (100 mg/day for three days followed by 20 mg/day) by patients with psoriatic arthritis improved responses
in all the Psoriatic Arthritis Response Criteria (PsARC) domains (joint pain, degree of swelling, and global assessment) by 29.2% (NNT: 3). It also increased the number of patients who reached ACR20 by 16.3% (NNT: 6) and improved the quality of life as measured by the Health Assessment Questionnaire (HAQ)36(A).

The rate of treatment discontinuation due to adverse events was greater with leflunomide (29.2%) than with methotrexate (10.8%), although the difference was not significant. The incidence of adverse events associated with leflunomide (38.7 events per 100 patients/year) was higher than for methotrexate (14.3 events per 100/year); leflunomide was also found to increase liver enzyme levels37(B). During 24 months of follow up, 33.3% of the patients discontinued treatment, 11.1% due to lack of efficacy and 23.3% due to the occurrence of adverse events38(B).

Sulfasalazine

After 24 weeks, patients with psoriatic arthritis who were treated with sulfasalazine (40 mg/kg/day) did not exhibit differences in pain, morning stiffness, global assessment of disease activity, or index of discontinuation compared to untreated patients39(B).

No benefits were found relative to pain, strength, number of affected joints, or joint swelling after 12 weeks of treatment with sulfasalazine (500 mg/day). The only measures that showed improvement were the patients’ and doctors’ global assessment of disease activity and the duration of morning stiffness40(B).

Treatment of psoriatic arthritis patients with sulfasalazine (2.0 g/day) over 24 weeks improved pain as assessed on VAS, but the treated patients did not differ from untreated patients with respect to morning stiffness, reduction in the number of affected joints, or score on the Ritchie Articular index. The most frequent adverse events associated with sulfasalazine were nausea, gastrointestinal disorders, headache, skin reactions, and increased liver enzyme and creatinine levels41(B).

**Recommendation 6**

The efficacy of methotrexate in the treatment of psoriatic arthritis is controversial; although this drug is sometimes used in combination with NSAIDs, its use should be carefully monitored due to the possibility of hepatotoxicity.

Cyclosporine is an efficacious option for the treatment of psoriatic arthritis, and its results may be potentiated by combination with adalimumab.

Leflunomide may be used in the treatment of psoriatic arthritis but should be carefully monitored due to its hepatotoxicity.

Sulfasalazine can be used in psoriatic arthritis to afford pain relief.

**7. What are the indications for the use of anti-tumour necrosis factor (TNF) agents in psoriatic arthritis?**

**Infliximab**

In patients who have had psoriatic arthritis for more than six months, therapeutic failure of disease-modifying anti-rheumatic drugs (DMARDs), peripheral polyarthritis, or morning stiffness lasting longer than 45 minutes, infliximab at a dose of 5 mg/kg/day at weeks 0, 2, 6, and 14 may improve ACR20, ACR50, and ACR70 responses42(A).

In patients who had psoriatic arthritis for more than six months, therapeutic failure with DMARDs or NSAIDs, peripheral polyarthritis, morning stiffness lasting longer than 45 minutes, or plaque psoriasis and who were free of tuberculosis, infections, cancer, and heart failure, treatment with infliximab at a dose of 5 mg/kg/day on weeks 0, 2, 6, 14, and 22, combined or not with methotrexate, affected their clinical progression43(A).

**Etanercept**

Treatment of patients with active psoriatic arthritis and inadequate response to NSAIDs may be performed with etanercept in 25 mg doses twice per week subcutaneously (SC) over 12 or 24 weeks, combined or not combined with methotrexate44,45(A).

**Adalimumab**

In adult patients with moderate to severe active psoriatic arthritis (at least three swollen and painful joints) or who have psoriatic skin lesions or a history of psoriasis, inadequate response or tolerance to NSAIDs, who are using or not using methotrexate, and who are without history of neurological symptoms suggestive of demyelinating disease, without history of active tuberculosis or listeriosis and without presence of severe infections, the use of 40 mg (SC) adalimumab on alternate weeks over 24 weeks of follow up can be assessed in relation to the ACR20 response at week 12 and the change in the Sharp score of structural damage on hand and foot x-rays at week 24. Other outcomes that may be assessed are ACR50, ACR70, response as measured by PsARC, HAQ-Disability Index (DI), SF-36 at weeks 12 and 24, and the occurrence of adverse events46(B).

In adult patients with moderate to severe active psoriatic arthritis (at least three swollen and painful joints) or who have chronic plaque psoriatic skin lesions or inadequate response to DMARDs in combination or without combination with methotrexate, who are without history of use of anti-TNF drugs or corticoids in the past four weeks, who are not using topical agents against psoriasis or phototherapy, who have not used alefacept or sipilizumab or any other biological agent in the past 12 weeks, who are without infection or history of tuberculosis, heart, kidney, neurological, psychiatric, endocrine, metabolic, or liver disease, and who are without symptoms of demyelination or cancer, treatment with 40 mg adalimumab on alternate weeks over 12 weeks may have an effect on the response measured by ACR20, ACR50, or ACR 7047(A).

**Golimumab**

In patients with active psoriatic arthritis and inadequate response to DMARDs or NSAIDs who are using or not using methotrexate, treatment with 50 or 100 mg golimumab every four weeks over a period of 20 weeks may increase the ACR20 response48(A).
Recommendation 7

Treatment with anti-TNF drugs (infliximab, etanercept, adalimumab, golimumab) is indicated in adult patients who have had moderate to severe active psoriatic arthritis (at least three swollen and painful joints) for more than six months and in those with chronic plaque psoriatic skin lesions or history of psoriasis and inadequate response or intolerance to NSAIDs or DMARDs over three months, combined or not with methotrexate.

8. Does the efficacy of various anti-TNF drugs differ in patients with psoriatic arthritis?

Patients with psoriatic arthritis and indication for treatment with anti-TNF drugs who were comparatively treated with infliximab (INF) at a dose of 5 mg/kg/day every 6-8 weeks, with 25 mg etanercept (ETN) twice per week, or with 40 mg adalimumab (ADA) on alternate weeks and were followed up over three months to one year exhibited ACR20 response rates of 72%, 70%, and 75% with ETN, ADA, and INF, respectively. No patient exhibited full remission (absence of clinically affected joints) after one year49(B). Table 1 shows the comparison of NNT in various anti-TNF drugs used in the treatment of PA.

Infliximab

In patients with psoriatic arthritis for more than six months, therapeutic failure with DMARDs, peripheral polyarthritis, and morning stiffness lasting more than 45 minutes, treatment with infliximab at 5 mg/kg at weeks 0, 2, 6, and 14 increased the ACR20 response rates by 55% (NNT: 2), ACR50 by 46% (NNT: 2), and ACR70 by 29% (NNT: 3). The patients’ responses were also measured as scores in the HAQ. The PsARC response exhibited a 54% increase (NNT: 2), the dactylitis score improved by 56% (NNT: 2), enthesis decreased by 17% (NNT: 6), and DAS28 improved by 43.2% (NNT: 2)46(A).

In patients with psoriatic arthritis for more than six months, therapeutic failure with DMARDs or NSAIDs, peripheral polyarthritis, morning stiffness lasting more than 45 minutes, and plaque psoriasis who were without tuberculosis, infections, cancer, or heart failure, treatment with infliximab at 5 mg/kg on weeks 0, 2, 6, 14, and 22 showed the following:

- A greater proportion of patients achieved ACR20 response at week 14 (47%) – NNT: 2 and at week 24 (38%) – NNT: 2. At week 14, 33% of the patients treated with infliximab exhibited a greater ACR50 response (NNT: 3), and 14% reached ACR70 (NNT: 7)41(A);
- At week 14, 50% of the patients treated with infliximab exhibited improved improvement as measured by PsARC (NNT: 2); at week 24, this was 38% (NNT: 3)40(A);
- The risk of dactylitis decreased by 12% (NNT: 8) and 22% (NNT: 5) at weeks 14 and 24, respectively. Enthesopathy decreased by 12% (NNT: 8) and 17% (NNT: 6) at weeks 14 and 24, respectively40(A);
- The proportion of patients who exhibited clinical response as measured by HAQ increased 40% (NNT: 3) and 32% (NNT: 3) at weeks 14 and 24, respectively41(A);
- These results persisted at week 5440(B);

After two years of follow up, the ACR20, ACR50, and ACR70 response rates were 45%, 45%, and 35%, respectively41(B).

The impact of treatment with infliximab on work capacity assessed at week 14 showed a 58.3% increase in productivity (NNT: 2), an 11.5-20% increase in the employment rate (NNT: 5-8), and a reduction in the number of lost work days6(A).

Etanercept

Treatment of patients with active psoriatic arthritis and indications for anti-TNF agents with 25 mg etanercept SC twice per week over 12 weeks increased the PsARC response rates by 64% (NNT: 2) and the ACR20 response rates by 60% (NNT: 2), reduced the number of affected joints by 53-70%, and increased the functional response (disability index score) by 29% (NNT: 3)46(A).

Patients with active psoriatic arthritis and inadequate response to NSAIDs were treated with 25 mg etanercept SC twice per week over 24 weeks. At week 12, the ACR20 response rate increased 44% (NNT: 2), and the PsARC response rate increased 47% (NNT: 2). At week 24, functional capacity improvement (HAQ) increased 48% (NNT: 2)46(A). Within 12 months, the ACR20 and PsARC response rates were 64% and 84%, respectively, and were thus similar to the values at week 1241(A). The patients treated with etanercept exhibited an increase of 47.2% in improvement measured by HAQ-DI at week 24, and 41.2% of the patients exhibited full response after 48 weeks40(B).

Adalimumab

In adults with moderate to severe active psoriatic arthritis, treatment with adalimumab resulted in a 44% increase in the ACR20 response rate at week 12 (NNT: 2). At week 24, the ACR20 response rate increased by 42% (NNT: 2). In patients treated with adalimumab, the response as measured by PsARC improved by 36% at week 12 (NNT: 3) and by 37% at week 24 (NNT: 3)46(B).

In patients using adalimumab, the ACR20, ACR50, and ACR70 response rates were 56%, 44%, and 30%, respectively, at week 48. The PASI50, PASI75, PASI90, and PASI100 response rates were 67%, 58%, 46%, and 33%, respectively41(B).

Relative to the quality of life and function measured by the Dermatology Life Quality Index (DLQI), the Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACT-Fatigue), the HAQ-DI, the Minimum Clinically Important Difference (MCID), the Physical Component Summary Score (PCS), and the SF-36, the patients treated with adalimumab for 24 weeks exhibited the following results: 23.6% achieved the MCID in HAQ-DI (≥ -0.3 point change from baseline) (NNT: 4); 20.9% achieved full resolution according to HAQ-DI (NNT: 5); 31.6% achieved the MCID in SF-36 (≥ 5 points) (NNT: 3); 31.6% achieved the MCID in FACIT (≥ 4 points) (NNT: 3); 31.3% achieved the MCID in DLQI (≥ -5 points); and 38.6% achieved full resolution according to DLQI (NNT: 3)46(B).

The percentages of patients who achieved responses according to ACR20, ACR50, ACR70, and PsARC after two years were 57.3%, 42.7%, 29.9%, and 63.5%, respectively; these rates are similar to those found at week 48. The percentage of patients who achieved a full response (HAQ-DI) was 38.5%, and...
the percentages of patients who achieved the MCID in HAQ-DI, SF-36, FACIT-F, and DLQI were 47.6%, 50.0%, 76.7%, and 56.3%, respectively; these values are also similar to those observed at week 48(B).

In patients with moderate to severe active psoriatic arthritis, treatment with 40 mg adalimumab in alternate weeks over 12 weeks increased the ACR20, ACR50, ACR70 response rates by 23% (NNT: 4), 23% (NNT: 4), and 14% (NNT: 7), respectively. The global activity of disease exhibited reduction, and the physical function (HAQ-DI) improved. The response was the same with or without combination of adalimumab with NSAIDs or corticoids. The (PsARC) response rate increased by 27% (NNT: 4), and scores of dactylitis and enthesitis decreased(A).

The ACR20/50/70 response rates were 65%, 43%, and 27%, respectively, and that of PsARC was 75%, similar to that found at week 12(A).

**Golimumab**

Patients with active psoriatic arthritis and inadequate response to DMARDs or NSAIDs who were treated with golimumab (50 or 100 mg) every four weeks over 20 weeks exhibited increased ACR20 response rates of 42% and 36%, respectively, at week 14, independently of combination with methotrexate. At week 14, the patients treated with golimumab at either dose also exhibited a 50% increase in (PsARC) response (NNT: 2) and a 40% increase in EULAR (DAS-28) response(A).

**Recommendation 8**

The efficacy of various anti-TNF drugs (infliximab, etanercept, adalimumab, and golimumab) relative to the treatment of patients with psoriatic arthritis does not differ, especially when response measures ACR20, PsARC, and HAQ are considered.

**9. Does the safety of various anti-TNF drugs differ in patients with psoriatic arthritis?**

**Infliximab**

The number of adverse events did not increase when infliximab was used. The most common adverse events were headache, bronchitis, respiratory infections, rhinitis, and skin rash(A).

The number of adverse events, severe adverse events, and infections did not increase in patients treated with infliximab (5 mg/kg at weeks 0, 2, 6, 14, and 22) compared to untreated patients. The proportion of instances of loss of adherence to treatment due to adverse events, including increased liver enzyme levels, was 4%. The most common adverse events were respiratory infection and headache; cancer may also occur(A).

**Etanercept**

The most common adverse event occurring in patients with psoriatic arthritis using 25 mg etanercept SC twice per week over 12 weeks was respiratory infection(A).

Patients with psoriatic arthritis and inadequate response to NSAIDs may be treated with 25 mg etanercept SC twice per week over 24 weeks combined or not with methotrexate. Adverse events may occur, including chest pain, kidney stones, syncope, and multiple sclerosis. The number of adverse events was not greater than in untreated patients. Most adverse events were moderate, and the most common event in up to two years of follow up was respiratory infection(A).

**Adalimumab**

At week 24 of treatment, adalimumab did not result in an increase in the number of adverse effects (respiratory infection, hypertension, and headache) compared to untreated patients. Severe adverse events included arthrosis, seizures, viral meningitis, kidney stones, pancreatitis, thrombocytopenia, and increased liver enzymes, any of which might lead to discontinuation of treatment(A). Adalimumab was shown to be safe at week 48(B).

The rate of adverse events in patients treated with adalimumab did not differ at two years compared to assessment at one year. Approximately 91.6% of the patients exhibited one adverse event, and 16.8% of them exhibited at least one severe adverse event. The most common adverse events were gallstones, myocardial infarction, appendicitis, urinary tract infection, osteoarthritis, seizures, kidney stones, tuberculosis, and lymphoma; approximately 6.7% of the patients discontinued treatment(B).

Adverse events at week 12 were mild in 26.7% of the patients, and most events were of moderate severity(A). Infection decreased by 15.1%, and no cases of tuberculosis, granulomatosis, demyelination, lupus, heart failure, or cancer occurred. At week 24, adverse events affected 54.6% of the patients. These events were severe in 3.1% and led to discontinuation in 6.2%. Other described adverse events include cough, nasopharyngitis, increased liver enzymes, lymphoma, and cancer(A).

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**Table 1 - Comparison of the NNT in various anti-TNF drugs used in the treatment of psoriatic arthritis.**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>ACR20</th>
<th>ACR50</th>
<th>ACR70</th>
<th>PsARC</th>
<th>HAQ</th>
<th>DAS 28</th>
<th>Enthesitis</th>
<th>DLQI</th>
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<td>3</td>
<td>2</td>
<td>6</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

NNT, number needed to treat; ACR, American College of Rheumatology Responders Index; PsARC, Psoriatic Arthritis Response Criteria; HAQ, Health Assessment Questionnaire; DAS-28, Disease Activity Score in 28 joints; DLQI, Dermatology Life Quality Index.
Golimumab

At week 14, the most common adverse events observed in patients with active psoriatic arthritis and inadequate response to DMARDs or NSAIDs combined or not with methotrexate who were treated with 50 or 100 mg golimumab every four weeks over 20 weeks were nasopharyngitis and respiratory infection. Infections occurred most frequently at higher doses. Approximately 3% of the instances of discontinuation of treatment were due to adverse events. Liver enzyme levels increased 18-24% and 13-34% in the patients who used 50 and 100 mg golimumab, respectively. Cancer and tuberculosis may occur and require treatment

Recommendation 9

Although it is difficult to quantify the occurrence of adverse effects, there are no significant differences in the safety profiles of the various anti-TNF drugs used in the treatment of psoriatic arthritis.

10. Is anti-TNF therapy able to reduce structural damage in patients with psoriatic arthritis?

Infliximab

Use of infliximab (5 mg/kg) at weeks 0, 2, and 6 and then every eight weeks until week 54 in patients with active psoriatic arthritis was assessed with respect to erosions and joint space narrowing on hand and foot x-rays by means of the modified Sharp/van der Heijde score. Treated patients showed less radiological progression at weeks 24 and 54 compared to untreated patients. After two years of follow up, the radiological progression in the treated patients was significantly lower than expected, and the adverse events remained within the range estimated in the first stage of treatment.

Patients with active psoriatic arthritis treated with 5 mg/kg infliximab at weeks 0, 2, 6, and 14 and then every eight weeks until week 50, as well as patients treated with the same dose at weeks 16, 18, and 22 and then every eight weeks until week 50, did not exhibit deterioration of radiological structural signs or progression of disease as measured by the Sharp/van der Heijde score in 85% and 84% of cases, respectively.

Etanercept

After 12 months of follow up, the radiological progression of disease exhibited a reduction of an average of −1.03 units in the Sharp score following use of etanercept. Combination with methotrexate did not change the results. Radiological progression was reduced corresponding to −1.38 unit in the total Sharp score after two years of follow up.

Adalimumab

Treatment with adalimumab induced significant inhibition of structural changes on radiographs. The average change in the total Sharp score from baseline to week 24 was 0.2 in the patients treated with adalimumab versus 1.0 in untreated patients.

Significant differences were also found in the erosion score. An average change of 0.0 was observed in the patients treated with adalimumab versus a change of 0.6 in patients who were not given treatment over the 24-week period. The score of joint space narrowing showed an average change of 0.2 in patients treated with adalimumab versus 0.4 in untreated patients over the 24-week period.

The changes in the Sharp score were 0.1 unit on average. The clinical and radiological responses were independent of combination with methotrexate.

After two years of treatment with 40 mg adalimumab on alternate weeks, 79.1% of patients exhibited reduction or no change in the Sharp score, similar to the results at weeks 24 and 48. Of the patients who had not shown radiological progression at week 48, 84.3% continued to demonstrate no radiological progression.

Assessment by magnetic resonance imaging of patients with active psoriatic arthritis without history of infections, severe disease, or demyelination and no previous use of anti-TNF drugs who were treated with 40 mg adalimumab on alternate weeks over 24 weeks showed 65% improvement in bone marrow swelling, no improvement in erosion score, 3% improvement in synovitis score, and 44% reduction in joint swelling.

Recommendation 10

Use of anti-TNF drugs in the treatment of psoriatic arthritis reduced the radiological progression of the disease, especially as measured by the Sharp score in patients who were monitored for up to two years.

11. Should conventional drugs such as methotrexate, leflunomide, and cyclosporine be used concomitantly with anti-TNF drugs?

Combination with DMARDs such as methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, intramuscular gold, penicillamine, or azathioprine did not modify the outcomes in patients with psoriatic arthritis who were treated with 5 mg/kg infliximab.

Treatment of patients with active psoriatic arthritis and indication for anti-TNF drugs with 25 mg etanercept SC twice per week over 12 weeks combined or not combined with methotrexate increased the PsARC and ACR20 response.

Patients with psoriatic arthritis treated with etanercept (25 mg twice per week) alone or combined with methotrexate (10-15 mg per week) exhibited similar survival rates after five years.

ACR20, ACR50, and ACR70 responses did not differ in patients treated with adalimumab alone or in combination with methotrexate.

The response of patients with moderate to severe active psoriatic arthritis to treatment with 40 mg adalimumab on alternate weeks over 12 weeks alone or combined with methotrexate or DMARDs (except for cyclosporine) was similar.

Patients with active psoriatic arthritis and inadequate response to DMARDs or NSAIDs treated with 50 or 100 mg...
golimumab every four weeks over 20 weeks exhibited increased ACR20 response independently of combination with methotrexate\textsuperscript{48}(A).

Treatment of patients with psoriatic arthritis over 12 months with cyclosporine (2.5-3.75 mg/kg/day) and adalimumab (40 mg on alternate weeks) resulted in similar PsARC responses in patients treated with adalimumab alone. However, the ACR50 response rates were higher (87%) with the combination compared to adalimumab alone (69%). There was also reduction in the combination of adalimumab doses (10%)\textsuperscript{35}(B).

**Recommendation 11**

The use of combinations of DMARDs such as methotrexate, cyclosporine, sulfasalazine, and leflunomide with anti-TNF drugs (infliximab, etanercept, adalimumab, golimumab) does not produce clinical results that differ from those obtained with the use of anti-TNF drugs alone in psoriatic arthritis.

**12. What is the evidence that supports switching anti-TNF drugs in patients with psoriatic arthritis?**

Between 25% and 33% of patients with psoriatic arthritis discontinue the use of the first anti-TNF drug after one year of treatment, usually due to the inefficacy of treatment or to adverse events. Inefficacy is cited as a cause increasingly often as treatment progresses, while adverse events are cited less often over time. No clinically significant difference in pain or functional (HAQ) outcome was found after treatment with the first, second, and third anti-TNF drugs used\textsuperscript{67}(B).

Approximately 33% of patients with psoriatic arthritis who were treated with anti-TNF drugs for periods of 6-70 months did not exhibit adequate response (61% due to lack of efficacy, 25% due to adverse events, and 14% due to loss of efficacy over time). Of the patients who switched to a second anti-TNF drug due to lack of efficacy, 92% exhibited adequate response, as did 60% of the patients who switched to a second anti-TNF drug due to adverse events and 50% of the patients who switched to a third anti-TNF drug. Approximately 70% of the patients who switched to a second or third anti-TNF drug due to loss of efficacy over time exhibited adequate response\textsuperscript{67}(B).

Following the use of 25 mg etanercept twice per week over 12 weeks and then 50 mg etanercept twice per week, 45.8% of patients with psoriatic arthritis who were previously treated with infliximab achieved PASI50, and 29.2% achieved PASI75 at week 24. Of the patients without previous use of biological agents, 92.3% and 73.8% achieved PASI50 and PASI75, respectively\textsuperscript{67}(B).

Of patients who completed 12 months of treatment, 75.5% continued the first anti-TNF drug, while 9.5% discontinued it due to inefficacy, 10.0% discontinued it due to adverse events, and 5.0% discontinued it for other reasons. The percentage of patients who maintained treatment with the first anti-TNF (infliximab, etanercept, or adalimumab) over the first and second years were 92% and 70%, respectively, and the percentage who maintained the first anti-TNF drug to which they were switched over the first and second years were 74% and 66%, respectively. One of the predictors of discontinuation and change in treatment was use of infliximab instead of etanercept [Hazard ratio (HR) = 2.8 after one year]\textsuperscript{64}(B).

Approximately 97% of patients with psoriatic arthritis who were treated with a first biological agent (infliximab, etanercept, or adalimumab) attained clinical response at week 12, and 90% of patients who required switching the anti-TNF drug achieved significant response. Approximately 40% of the patients who required switching due to lack of response responded to the second-line agent, and half responded to the third course of treatment\textsuperscript{64}(B).

Approximately 67% of patients with psoriatic arthritis switched from infliximab to etanercept. After three months of treatment with etanercept, the proportion of patients who achieved PsARC response increased from 10-70% (NNT: 2), and the HAQ score decreased. Approximately 46% of patients with psoriatic arthritis switched from etanercept to adalimumab. After three months of treatment with adalimumab, the proportion of patients who achieved PsARC response increased from 14.3-57.1% (NNT: 2)\textsuperscript{145}(B).

Patients with psoriatic arthritis using anti-TNF drugs (infliximab, etanercept, or adalimumab) exhibited 87% adherence/response, and the response of patients who switched to a second anti-TNF drug was 81%. The rate of response/adherence was better among patients who switched to the second anti-TNF drug due to adverse events (HR for discontinuation = 0.55) and among patients treated with infliximab (HR= 3.22)\textsuperscript{64}(B).

**Recommendation 12**

Switching anti-TNF drugs in patients with psoriatic arthritis exhibiting adverse events or inadequate response is usually met by a satisfactory therapeutic response.

**13. How long should an anti-TNF drug be used in the treatment of patients with psoriatic arthritis?**

In patients with psoriatic arthritis treated with etanercept SC (50 mg twice per week over 12 weeks followed by 25 mg twice per week), the clinical response assessed by means of DAS28, painVAS, and PASI was as follows\textsuperscript{48}(B):

- After 48 weeks of treatment: 76.8% reduction of pain (VAS); 44% reduction of the DAS28 score; 83% reduction of the PASI50 score, 78% reduction of the PASI75 score, and 43% reduction of the PASI90 score, with average PASI of 70%.
- After 96 weeks of treatment: 89.6% reduction of pain (VAS); 57% reduction in the DAS28 score; 87% reduction of the PASI50 score, 81% reduction of the PASI75 score, and 65% reduction of the PASI90 score, with average PASI of 82%.
- After 144 weeks of treatment: 94.7% reduction of pain (VAS); 67% reduction of the DAS28 score; 96% reduction of the PASI50 score, 92% reduction of the PASI75 score, and 66% reduction of the PASI90 score, with average PASI of 74%.

The ACR20 responses of patients with psoriatic arthritis treated with infliximab at three months, one year, and two years were 79%, 61%, and 80%, respectively; the corresponding results for patients treated with etanercept were 76%,
80%, and 90%. The ACR50 responses of patients with psoriatic arthritis treated with infliximab at three months, one year, and two years were 64%, 39%, and 40%, respectively; the corresponding results for patients treated with etanercept were 49%, 65%, and 68%\(^{(4)}\).

After five years of treatment with infliximab (5 mg/kg intravenously) at weeks 0, 2, and 6 and then every eight weeks, the percentage of patients who achieved PsARC was 60%, PASI70 was 66.7%, PASI90 was 63.3%, and ACR50 was 56.7%. In patients treated with etanercept (25 mg SC) twice per week, the percentage who achieved PsARC was 64%, PASI70 and PASI90 was 68%, and ACR50 was 56%. The percentages of response to treatment with adalimumab (40 mg SC) on alternate weeks were PsARC 56%, PASI70 58%, PASI90 50%, and ACR50 50%. At the end of treatment, the survival rate of patients treated with infliximab was 56.7%, etanercept was 76%, and adalimumab was 50%\(^{(5)}\).Episodes of remission in patients with psoriatic arthritis treated with anti-TNF increased by 17% after six years of follow-up; the average length of remission was 13 ± 9.4 months. The frequency of remission during the period without treatment increased 60% in patients treated with anti-TNF drugs compared to the frequency of remission in patients treated with methotrexate. The length of remission following discontinuation of treatment was 12 ± 2.4 months\(^{(6)}\).

The percentages of patients treated with adalimumab who achieved ACR20, ACR50, ACR70, and PsARC responses after two years were 57.3%, 42.7%, 29.9%, and 63.5%, respectively, similar to the results at week 48. Full response (HAQ-DI) was achieved by 38.5% of the patients, and the percentage of patients who achieved MCID in HAQ-DI, SF-36, FACIT-F, and DLQI was 47.6%, 50.0%, 76.7%, and 56.3%, respectively, also similar to the results at week 48\(^{(7)}\).

The percentage of patients with active psoriatic arthritis treated with 25 mg etanercept SC twice per week over two weeks who achieved ACR20 increased by 44% (NNT: 2), and the percentage who achieved PsARC increased by 47% (NNT: 2) at week 12. At week 24, functional capacity improvement (HAQ) increased by 48% (NNT: 2)\(^{(8)}\). After 12 months, the ACR20 and PsARC response rates were 64% and 84%, respectively, similar to the results at week 12\(^{(9)}\). Patients treated with etanercept exhibited 47.2% improvement as measured by HAQ-DI at week 24, and 41.2% of the patients exhibited full response at week 48\(^{(10)}\).

The proportion of patients with psoriatic arthritis treated with infliximab (5 mg/kg) on weeks 0, 2, 5, 14, and 22 who achieved ACR20 at week 14 (48% - NNT: 2) and at week 24 (38% - NNT: 2) was higher. At week 14, 33% of the patients treated with infliximab achieved ACR50 response (NNT: 3), and 14% achieved ACR70 (NNT: 7)\(^{(11)}\). These results persisted until week 54\(^{(12)}\). After two years of follow up, the ACR20, ACR50, and ACR70 response rates were 45% and 35%, respectively\(^{(13)}\).

**Recommendation 13**

Treatment of psoriatic arthritis with anti-TNF drugs for more than six years shows stability of the efficacy and safety achieved in the first year. Treatment might be discontinued when signs of remission appear; on average, remission lasts for 12 months.

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### 14. Is there evidence that supports the use of biological agents with other mechanisms of action in psoriatic arthritis?

**Ustekinumab**

Treatment of patients with active psoriatic arthritis with 90 mg ustekinumab every week over four weeks increased the percentage of ACR20, ACR50, and ACR70 response by 28% (NNT: 4), 18% (NNT: 6), and 11% (NNT: 9), respectively, at week 12. However, at weeks 24, 28, and 36, the rates of clinical response did not increase\(^{(14)}\).

After 12 weeks of treatment with ustekinumab, patients with psoriatic arthritis exhibited 88% reduction in HAQ-DI, 99% reduction in DLQI, and the number of patients with score 0 or one in DLQI increased by 53%\(^{(15)}\). Ustekinumab may be associated with a favorable response of the skin component of disease regardless of the presence of joint response.

**Abatacept**

After six months of treatment with abatacept at a dose of 30/10 mg/kg, the percentage of patients who achieved ACR20 increased by 23%; this percentage increased by 29% at a dose of 10 mg/kg. The ACR50 and ACR70 response rates were 25% and 13%, respectively, at 10 mg/kg. The ACR20 response rate at a dose of 10 mg/kg increased by 25% in patients who had never used anti-TNF drugs (NNT: 4)\(^{(16)}\).

**Recommendation 14**

Currently, there is no evidence supporting the use of non-anti-TNF biological agents in the treatment of patients with psoriatic arthritis.

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### 15. Is there any evidence for the efficacy of the medications used in the treatment of skin psoriasis with respect to the articular and periarticular manifestations of psoriatic arthritis?

In patients with moderate to severe stable plaque psoriasis affecting at least 10% of the body surface and in patients with active psoriatic arthritis, treatment with etanercept (50 or 100 mg per week over 12 weeks followed by 50 mg over a further 12 weeks) led to 62%-70% skin improvement as measured by PASI75, to 70%, 50%, and 35% improvement in arthritis response measured by ACR20, ACR50, and ACR70, respectively, and to reduction in dactylitis and enthesitis scores. Analysis of combined outcomes [Euro-Qol (EQ-5D®), PASI, and ACR50] showed that treatment benefited 31% of patients\(^{(17)}\).

Most of the agents used in the treatment of psoriasis (adalimumab, infliximab, etanercept, methotrexate, and cyclosporine) are also used in the treatment of psoriatic arthritis. These biological agents are the medications with the best efficacy and fewest adverse events, and they produce concomitant skin and joint improvement. Patients with moderate to severe psoriasis and history of psoriatic arthritis who were treated with adalimumab exhibited 83% reduction in the...
pain VAS at week 16. The concomitant (PASI and ACR20) response increased by 99% at week 16\(^{77}\)A).

**Recommendation 15**

Concomitant or combined skin and joint responses are usually detected with treatments for psoriatic arthritis that employ anti-TNF agents.

**Conflicts of interest**

Carneiro S: Member of the MSD laboratory board. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Janssen, MSD, and Pfizer laboratories.

Azevedo VF: Consultant for the Abbott, Janssen, Pfizer, and Roche laboratories. Lectures and participation in conferences, symposia, and meetings were funded by Abbott, Bristol-Myers-Squibb, Janssen, MSD, and Roche laboratories. The author also participated as an investigator in clinical trials conducted in Brazil by the BMS, Galen Research, Roche, and UCB laboratories.

Bonfiglioli R: Board member of the Abbott, MSD, and Pfizer laboratories. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Actelion, Janssen, MSD, Pfizer, and Roche laboratories. The author is a primary investigator and/or sub-investigator in clinical trials conducted in Brazil by the Bristol-Myers-Squibb, MSD, and Roche laboratories.

Ranza R: Board member of the Abbott, MSD, and Pfizer laboratories. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Janssen, MSD, Pfizer and Roche laboratories. The author is a primary investigator in clinical trials conducted in Brazil by the Roche laboratory.

Gonçalves CR: Board member of the Abbott, Janssen, MSD, Pfizer, and Roche laboratories. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Aché, Aventis, Janssen, MSD, and Pfizer laboratories. The author is an investigator in clinical trials conducted in Brazil by the Roche laboratory.

Keiserman M: Consultant for the Abbott, MSD, and Pfizer laboratories. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Actelion, Janssen, MSD, Pfizer, and Roche laboratories. The author is an investigator in clinical trials conducted in Brazil by the Bristol-Myers-Squibb, MSD and Roche laboratories.

Meirelles ES: Board member of the Janssen and Pfizer laboratories. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, AstraZeneca, Janssen, Lilly, MSD, Pfizer, Roche, Sanofi-Aventis, and Servier laboratories. The author is a principal investigator in clinical trials conducted in Brazil by the Novartis, and Roche laboratories.

Pinheiro MM: Board member of MSD. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Janssen, Novartis, MSD, Pfizer, and Roche laboratories. The author is a principal investigator in clinical trials conducted in Brazil by the Novartis, and Roche laboratories.

Ximenes AC: Board member of the Bristol, MSD, and Pfizer laboratories. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Aché, Janssen, Pfizer and Roche laboratories. The author is a principal investigator in clinical trials conducted in Brazil by the MSD, Pfizer, Roche, and UCB laboratories.

Bernardo W: declares no conflicts of interest.

Sampaio-Barros PD: Board member of the Abbott, MSD, and Pfizer laboratories. Lectures and participation in conferences, symposia, and meetings were funded by the Abbott, Actelion, Janssen, MSD, Pfizer, and Roche laboratories. The author is a principal investigator in clinical trials conducted in Brazil by the Roche laboratory.

**Appendix**

**Question 1**

What are the criteria on the basis of which an individual is considered to have psoriatic arthritis?


**Question 2**

Are there correlations among skin, nail, and joint disease activity in psoriatic arthritis?


**Question 3**

What are the comorbidities most often associated with psoriatic arthritis?


**Question 4**

What is the evidence regarding the use of corticosteroids in patients with psoriatic arthritis?

(“Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis”) AND (“Steroids OR Androstanols OR Androstanediols” OR “Cardenolides OR Cardenolides” OR “Cardiac Glycosides OR Sterols OR Cyclosteroids OR Estranes OR Estrenes OR Gonanes OR Homosteroids OR Testolactone OR “Hydroxysteroids OR Ketosteroids OR 17-Ketosteroids OR Norsteroids OR Norandrostanes OR Norpregnanes OR Preg-
nanes OR Pregnanediol OR Pregnanediones OR Pregnanetriol OR Pregnanolone OR Pregnanatrienes OR Pregnanetriol OR Pregnanediol OR Chlormadinone OR Cyproterone OR Florinated OR Betamethasone OR Dexamethasone OR Flumethasone OR Fluocinolone OR Fluocortolone OR Fluorometholone OR Fluoxidymesterone OR Fluprednisolone OR Flurandrenolone OR Flugestone OR Paramethasone OR Triamcinolone OR Prednisolone OR Hydrocortisone OR Corticosteroids OR Mineralocorticoids OR Glucocorticoids OR Hydroxycorticosteroids)

Question 5

What is the evidence regarding the use of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (Anti-Inflammatory Agents OR Cyclooxygenase 2 OR COX-2 OR rofecoxib OR Ibuprofen OR celecoxib OR Naproxen OR Acetaminophen OR NSAID OR paracetamol OR parecoxib OR diclofenac OR aspirin OR meloxicam OR acetylsalicylic OR piroxicam) AND (randomised controlled trial[Publication Type] OR (randomised[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]))

Question 6

What is the evidence regarding the use of the conventional drugs methotrexate, cyclosporine, leflunomide, and sulfasalazine in patients with psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (methotrexate OR leflunomide OR sulfasalazine OR gold sodium OR hydroxychloroquine OR ciclosporin) AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])

Question 7

What are the indications for the use of anti-tumour necrosis factor (TNF) agents in psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (Tumor Necrosis Factor-alpha OR golimumab OR infliximab OR adalimumab OR etanercept) AND (randomised controlled trial[Publication Type] OR (randomised[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]))

Question 8

Does the efficacy of the various anti-TNF drugs differ in patients with psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (Tumor Necrosis Factor-alpha OR golimumab OR infliximab OR adalimumab OR etanercept) AND (randomised controlled trial[Publication Type] OR (randomised[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]))

Question 9

Does the safety of various anti-TNF drugs differ in patients with psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (Tumor Necrosis Factor-alpha OR golfimub OR infliximab OR adalimumab OR etanercept) AND (radio-graph* OR damage OR structur* OR joint OR imag*)

Question 10

Is anti-TNF therapy able to reduce structural damage in patients with psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (Tumor Necrosis Factor-alpha OR golfimub OR infliximab OR adalimumab OR etanercept) AND (radio-graph* OR damage OR structur* OR joint OR imag*)

Question 11

Should conventional drugs such as methotrexate, leflunomide, and cyclosporine be used concomitantly with anti-TNF drugs?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (Tumor Necrosis Factor-alpha OR golfimub OR infliximab OR adalimumab OR etanercept) AND (methotrexate OR leflunomide OR sulfasalazine OR gold sodium OR hydroxychloroquine OR ciclosporin)

Question 12

What is the evidence that supports switching anti-TNF drugs in patients with psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND switch*)

Question 13

How long should an anti-TNF drug be used in the treatment of patients with psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (Time OR follow-up OR cohort)

Question 14

Is there evidence that supports the use of biological agents exhibiting other mechanisms of action in psoriatic arthritis?

(Arthritis, Psoriatic OR Psoriasis Arthropathica OR Arthritic Psoriasis) AND (rituximab OR tocilizumab OR abatacept OR Antibodies, Monoclonal) AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])

Question 15

Is there evidence for the efficacy of the medications used in the treatment of skin psoriasis relative to the articular and periarticular manifestations of psoriatic arthritis?

“Arthritis, Psoriatic”[Mesh] AND “Psoriasis”[Mesh] AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clini-
REFERENCES


