Biological Therapy for Psoriatic Arthritis in Clinical Practice: Outcomes Up to 2 Years

LIISA M. VIRKKI, BINDU C. SUMATHIKUTTY, MERJA AARNIO, HEIKKI VALLEALA, RIITTA HEIKKILÄ, MARKKU KAUPPI, KRISTA KARSTILA, LAURA PIRILÄ, PÄIVI EKMAN, SIRPA SALOMAA, MATTI ROMU, JOUKO SEPPÄLÄ, HELENA NIINISALO, YRJÖ T. KONTTINEN, and DAN C. NORDSTRÖM

ABSTRACT. ***Objective.*** To evaluate the performance of biological drugs in psoriatic arthritis (PsA) in a routine care setting, using the Finnish national register of biological treatment (ROB-FIN).

Methods. Patients with PsA who started therapy with infliximab or etanercept between June 2000 and February 2006 (n = 127) were followed for up to 24 months. Response was evaluated using American College of Rheumatology response criteria including individual measures.

Results. Significantly diminished values for swollen and tender joints, patient's global and pain assessments, doctor's global assessment of disease activity, erythrocyte sedimentation rate, C-reactive protein, and Health Assessment Questionnaire score were observed within 3 months after commencement of both infliximab and etanercept. Values remained significantly lower throughout the 24 months of followup. ACR20 response at 3 months was 79% (n = 22/28) for infliximab and 76% (n = 34/45) for etanercept. The first biological drug was discontinued in 16% due to lack of effectiveness and in 6% due to adverse events.

Conclusion. Anti-tumor necrosis factor-α therapy, often combined with conventional disease-modifying antirheumatic drugs, appeared to have limited toxicity and persistent effectiveness for up to 2 years in a cohort of Finnish patients with severe peripheral PsA. (J Rheumatol First Release August 15 2010; doi:10.3899/jrheum.091477)

Key Indexing Terms:
PSORIATIC ARTHRITIS BIOLOGIC AGENTS COMBINATION THERAPY

From the University of Helsinki, Helsinki; Helsinki University Central Hospital, Helsinki; Rheumatism Foundation Hospital, Heinola; Päijät-Häme Central Hospital, Lahti; Tampere University Central Hospital, Tampere; Loimaa Regional Hospital, Loimaa; Rauma Regional Hospital, Rauma; Lapland Central Hospital, Rovaniemi; Kanta-Häme Central Hospital, Hämeenlinna; Kuopio University Hospital, Kuopio; ORTON Orthopaedic Hospital of the Invalid Foundation, Helsinki; and COXA Hospital for Joint Replacement, Tampere, Finland.

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L.M. Virkki, MSc; B.C. Sumathikutty, BDS, University of Helsinki; M. Aarnio, MD; H. Valleala, MD, PhD; R. Heikkilä, MD, Helsinki University Central Hospital; M. Kauppi, MD, PhD, Rheumatism Foundation Hospital, Päijät-Häme Central Hospital; K. Karstila, MD, PhD, Tampere University Central Hospital; L. Pirilä, MD, PhD, Loimaa Regional Hospital; P. Ekman, MD, Rauma Regional Hospital; S. Salomaa, MD, Lapland Central Hospital; M. Romu, MD, Helsinki University Central Hospital; J. Seppälä, MD, Kanta-Häme Central Hospital; H. Niinisalo, MD, Kuopio University Hospital; Y.T. Konttinen, MD, PhD, University of Helsinki, Helsinki University Central Hospital, ORTON Orthopaedic Hospital of the Invalid Foundation, COXA Hospital for Joint Replacement; D.C. Nordström, MD, PhD, University of Helsinki, Helsinki University Central Hospital.

Address correspondence to Dr. D.C. Nordström, Helsinki University Central Hospital, Haartmaninkatu 4, 00290 Helsinki, Finland. E-mail: dan.nordstrom@hus.fi

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Psoriatic arthritis (PsA) is a chronic, heterogeneous disease characterized by inflammation of the joints, tendons, and entheses. It may lead to functional impairment and considerable reduction in the patient's quality of life[1,2]. Conventional drug therapy of PsA has mainly consisted of nonsteroidal antiinflammatory drugs (NSAID), intraarticular steroids, and disease modifying antirheumatic drugs (DMARD), of which methotrexate (MTX), sulfasalazine (SSZ), cyclosporine (CSA), and leflunomide (LEF) alone or in combination are the most widely used. However, evidence of the clinical benefit of DMARD therapy in treatment of PsA is largely inconclusive[3,4].

The advent of biological tumor necrosis factor-α (TNF-α) inhibitors has led to substantial improvement in management of severe and active PsA refractory to conventional DMARD. The efficacy of these agents has been demonstrated in randomized controlled trials (RCT)[5,6,7,8]. The medium to longterm outcomes in the routine care setting need to be ascertained. To evaluate the effectiveness and adverse events (AE) of biological therapies in the treatment of inflammatory arthritides, the Finnish Society for Rheumatology has set up a national register of biological treatment (ROB-FIN)[9,10,11,12,13], maintained with approval from the Internal Medicine Ethics Committee of the

Hospital District of Helsinki and Uusimaa. We report on the utilization and performance of biologicals in the treatment of PsA for up to 2 years in clinical practice.

MATERIALS AND METHODS

Patients. Inclusion in the ROB-FIN register requires informed consent from the patient receiving biological therapy for inflammatory arthritis. Patients starting biological therapy between June 2000 and February 2006 were included in our study (1) if the patient had been diagnosed with psoriatic arthritis; and (2) if a baseline report, i.e., patient demographic data and disease profile at commencement of biological therapy, had been filed. No other inclusion or exclusion criteria were imposed. Patients were followed for up to 24 months. Data collection for the present study ended in February 2008, while the data were extracted in April 2009 to account for a possible lag time of incoming reports.

The treatment and followup of patients with PsA using biologicals occurs mainly in outpatient rheumatology clinics of central or regional hospitals. During the period of data collection, evidence-based national and international treatment guidelines and recommendations for the management of PsA were only emerging[14,15,16,17]. Patient selection for biological therapy of PsA with peripheral arthritis has, presumably, been based on the national evidence-based treatment recommendations (the so-called Current Care guidelines) for rheumatoid arthritis (RA)[18], but with modification based on the clinical judgment of a specialist to accomodate individual patient needs. The Finnish Current Care guidelines for RA consider the patient eligible for biological therapy if he/she suffers from severe and continuously active disease, having swollen and tender joint counts ≥ 6, and morning stiffness > 45 minutes and/or erythrocyte sedimentation rate (ESR) ≥ 30 mm/h and/or C-reactive protein (CRP) ≥ 28 mg/l, and if response to conventional DMARD and combinations thereof is not satisfactory. Continuation of treatment is warranted if he/she responds favorably to the biological drug, reaching an American College of Rheumatology 50% (ACR50) response by 3 months of therapy. Special consideration for axial and/or enthesitic involvement is not apparent from the register data for the present cohort, which is a possible limitation of this study.

Assessments. ROB-FIN register data consist of parameters needed for assessment of disease activity and response to treatment. The data include all parameters needed to assess ACR response: swollen and tender joint counts, patient's global and pain assessments, doctor's global assessment of disease activity, ESR, CRP, and assessment of functional status (Health Assessment Questionnaire; HAQ). A 54 swollen joint and 53 tender joint index is used for all ROB-FIN patients with inflammatory arthritides. The distal interphalangeal joints, which are frequently involved in PsA, are not included in the indices, which is a limitation of this study. Demographic factors, concomitant medication, and dosages are also recorded. Data on AE include a description of the event and evaluation of its severity (mild, moderate, serious, life-threatening, and fatal; disablement, malignancy, and hospitalization), the measures taken regarding the usage of the biological, and the outcome of the AE as reported in detail earlier[10]. The register data are provided by Finnish rheumatologists on a continuous, regular basis using structured forms available from the Website of the Finnish Society for Rheumatology. Reporting occurs at baseline and subsequently at prespecified intervals during therapy (at 3 and 6 months, and semiannually thereafter), and on discontinuation of therapy. In the present study, patients were followed for up to 24 months, with response assessments at 3, 12, and 24 months of therapy.

Statistics. Data were analyzed with SPSS software, version 15.0 (SPSS, Chicago, IL, USA). Variable descriptives were checked for possible extreme values or errors in data input. Baseline demographics and disease characteristics were assessed using frequency calculations and descriptive statistics. Changes in the swollen and tender joint counts, patient's global and pain assessments, doctor's global assessment, ESR, CRP, and HAQ during 24 months of followup were tested for significance with the Friedman test. A statistically significant overall result was achieved by pairwise Wilcoxon signed-ranks testing. The same method was used for the number of concomitant DMARD and prednisone-equivalent dosages of corticosteroid. Use of NSAID, analgesics, oral corticosteroid, and DMARD at different times during the followup was compared with Friedman and/or Cochran's Q tests, for assessment of trends in the usage (continuously, temporarily as needed, or not used) and absolute usage (yes/no), respectively. In case of a statistically significant overall result, pairwise Wilcoxon signed-ranks and/or Sign and McNemar testing was performed, respectively. Categorical data were compared with chi-square or Fisher's exact test, as appropriate. The significance level (p value) was set at 0.05 in all statistical testing.

RESULTS

Patient demographics and concomitant medication. In total, 127 patients fulfilled the inclusion criteria for this study (Figure 1). Patient demographics are presented in Table 1. The biological drug at baseline was infliximab in 39, etanercept in 76, adalimumab in 10, and anakinra in 2. Generally, standard dosages of etanercept, adalimumab, and anakinra (prescribed off-label) were used, i.e., etanercept 25 mg subcutaneously (SC) twice weekly, adalimumab 40 mg SC every 2 weeks, anakinra 100 mg SC once daily. The recommended dosage of infliximab for treatment of PsA is 5 mg/kg intravenously (IV) at 0, 2, and 6 weeks and then every 8 weeks. Compared to this, initial doses in the present cohort were often relatively low — 200 mg in 22 patients. Some dose escalations, e.g., from 200 mg to 300 mg, occurred later (n = 12), while dose reductions, from 300 mg to 200 mg, were less frequent (n = 4).

The biologicals were combined with oral corticosteroid and DMARD throughout the 24-month followup. At baseline, 40% used oral corticosteroid continuously, and 84% used at least one concomitant DMARD. Overall, MTX, SSZ, CSA, and LEF were the most frequently used concomitant DMARD, prescribed to 51%, 20%, 18%, and 11%, respectively (Table 2). Less frequently used DMARD were sodium aurothiomalate (8%), hydroxychloroquine (7%), podophyllotoxin derivative (6%), azathioprine (2%), and auranofin (1%).

NSAID and analgesics were used continuously or temporarily as needed by 78% and 15% of patients, respectively; 14% did not use pain medication.

The number of concomitant DMARD used decreased during the followup. Statistically significant decreases were found for patients taking etanercept (Table 3). However, no specific DMARD accounted distinctively for the decrease in the DMARD number. As well, NSAID usage decreased during the followup, significantly so in patients taking etanercept. At baseline, NSAID was used continuously by 47% and not at all by 15% of etanercept users. After 24 months, the corresponding figures were 12% and 33%, respectively (Table 3). Use of analgesics did not change significantly; neither did use of oral corticosteroid per se, but the dosage decreased significantly within 3 months after commencement of infliximab ($p < 0.05$), from a median prednisone-

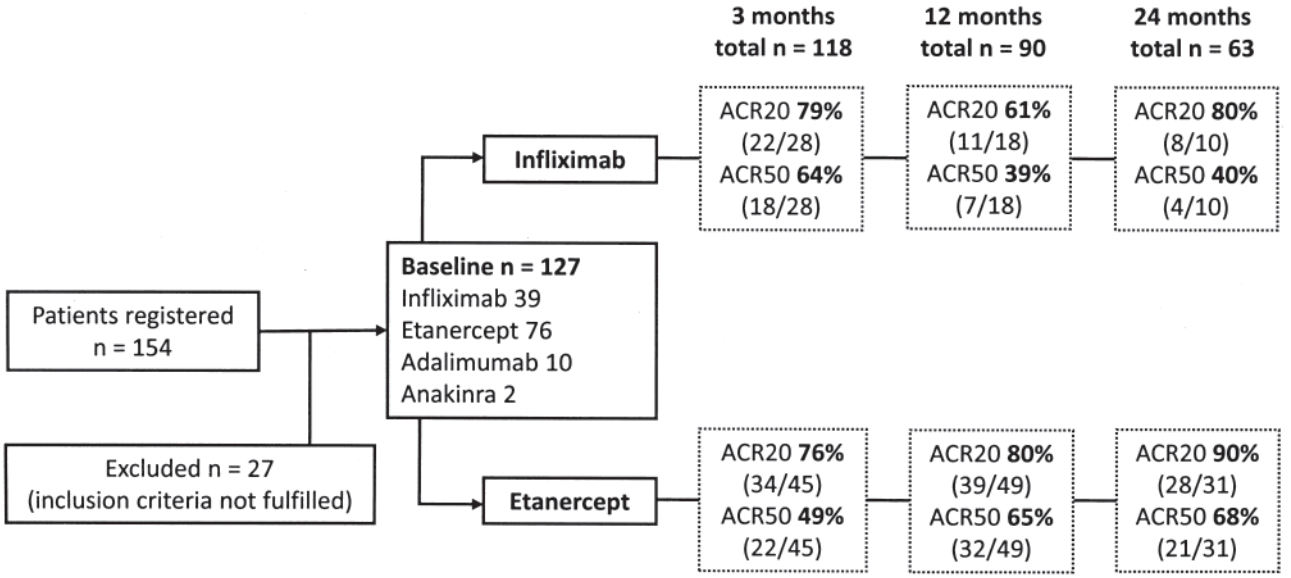

Figure 1. The patients registered, and proportions of patients receiving infliximab or etanercept who achieved ACR20 and ACR50 response at 3, 12, and 24 months. Calculations are per-protocol based on patients with a filed report at the relevant timepoint and with sufficient data for assessment of ACR response.

equivalent dose of 7.5 mg at commencement to 5 mg at all later times. The dosage also decreased in patients taking etanercept, although the median dose was 5 mg from baseline onward.

Performance of biologicals. A significant reduction of the values for swollen and tender joints, patient's global and pain assessments, doctor's global assessment, ESR, CRP, and HAQ was observed within 3 months after commencement of both infliximab and etanercept ($p < 0.001$). The values remained significantly lower throughout the 24 months of followup (Figure 2). Patients who started biological therapy with infliximab had a more severe disease status at baseline than those who started with etanercept ($p < 0.05$ for swollen joint count, ESR, CRP, and doctor's global). As patients were not randomized to receive these agents, and the baseline values differed in the 2 groups, any comparisons between the 2 agents should be interpreted with caution.

Of the patients receiving infliximab and etanercept, 28 and 45, respectively, had sufficient data for calculation of ACR response criteria at 3 months; of these, 79% (n = 22) and 76% (n = 34), respectively, fulfilled ACR20, and 64% (n = 18) and 49% (n = 22) fulfilled ACR50 (Figure 1). Of the patients taking infliximab and etanercept who had a documented report from their 3-month visit, only 4 and 7, respectively, could not be assessed for ACR response due to missing data on some ACR measures. In addition, as the non-missing measures did not differ statistically significantly from those of the assessable patients, no systematic bias in the response assessment was apparent.

Notably, of the ACR50 nonresponders, the majority continued to receive biological therapy beyond 3 months (see "Patients," above). Corresponding ACR response figures at 12 and 24 months are presented in Figure 1. Use of MTX or oral corticosteroid was not associated with higher response rates. As well, no statistically significant association was found between the number of concomitant DMARD and response rates.

Statistics on adalimumab and anakinra are not included due to the small number of patients treated with these agents at the time of data collection.

Reasons for discontinuation of the first biological drug. Of the 127 patients, 46 (36%) had discontinued their first biological drug within the first 2 years (according to the assumptions specified below), and 18 patients (14%) had been lost to followup.

Twenty patients (16%) discontinued the first biological drug due to lack of effectiveness, as specifically reported by the attending rheumatologist (n = 8) or as assumed based on primary or secondary ACR50 nonresponse (n = 12; see "Patients," above). The discontinued agent was infliximab in 9 patients, etanercept in 7, adalimumab in 3, and anakinra in one (the total numbers on each agent are given in Figure 1).

Nineteen patients (15%) were reported to have experienced an AE of their first biological drug within the first 2 years of treatment. AE led to discontinuation of the drug in 8 cases (6%). AE leading to discontinuation of infliximab were infusion reaction, urticaria, eczema, acute myeloid leukemia, and suspicion of multiple sclerosis (MS); the patient was subsequently diagnosed with MS. One further patient discontinued infliximab due to an unspecified AE. One patient discontinued etanercept due to myocardial infarction, and one patient discontinued anakinra due to leukocytopenia and elevated alanine aminotransferase.

Table 1. Patient demographics at baseline.

Age, yrs	
Median	50
IQR	42–56
Range	20–73
Men, %	59.1
Years since diagnosis, n = 98	
Median	11
IQR	6–18
Range	0–35
Swollen joints, n = 124	
Median	6
IQR	3–11
Range	0–30
Tender joints, n = 123	
Median	7
IQR	4–13
Range	0–35
Patient's global (100 mm VAS), n = 121	
Median	59
IQR	42–75
Range	3–100
Pain (100 mm VAS), n = 123	
Median	62
IQR	45–75
Range	3–100
HAQ score, n = 114	
Median	1.0
IQR	0.63–1.5
Range	0–3
ESR, mm/h, n = 123	
Median	29
IQR	13–62
Range	2–100
CRP, mg/l, n = 122	
Median	20
IQR	6–43
Range	1–218
Doctor's global (100 mm VAS*), n = 118	
Median	50
IQR	45–75
Range	5–100
No. concomitant DMARD (n = 125), %	
0	16.0
1	48.8
2	29.6
3	5.6
Continuous use of oral corticosteroid (n = 125), %	40.0
Use of NSAID (n = 125), %	
Continuously	43.2
Temporarily as needed	35.2
Not used	21.6
Use of analgesics (n = 125), %	
Continuously	8.8
Temporarily as needed	6.4
Not used	84.8

IQR: interquartile range; VAS: visual analog scale; HAQ: Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; DMARD: disease modifying antirheumatic drug; NSAID: nonsteroidal antiinflammatory drug. * Up to year 2004, register forms had a 5-grade Likert scale, which has been converted to 100-mm VAS: grade 1: 0 mm, grade 2: 25 mm, grade 3: 50 mm, grade 4: 75 mm, grade 5: 100 mm.

One patient discontinued etanercept due to remission. Seventeen patients discontinued their first biological drug due to some other or unspecified reason. Specified reasons were (1) discontinuation of infliximab due to resolved synovitis but active psoriatic skin disease (referred to a dermatologist); (2) switching infliximab to etanercept due to problems with IV infusions due to bad veins; and (3) discontinuation of etanercept due to elective surgery and subsequent clinical remission. The other discontinuations were unspecified, and consisted of switches from infliximab to etanercept or adalimumab (n = 9) or from etanercept to adalimumab (n = 5).

DISCUSSION

Due to the limited evidence supporting longterm biological therapy for PsA in routine care settings, clinicians are strongly encouraged to register this kind of patient in national registers to collect information on outcome and toxicity[14]. Using the ROB-FIN register, it was shown that infliximab or etanercept, often in combination with conventional DMARD, induced a favorable response in a cohort of Finnish patients with PsA within 3 months, which persisted up to 24 months. The ACR20 responses at 3 months (79% for infliximab and 76% for etanercept) are encouraging and are in agreement with results of RCT. In the IMPACT 2 study, an ACR20 response was observed in 58% of infliximab ± MTX treated patients at Week 14[5]; and in 2 studies performed by Mease and coworkers[6,7], 73% and 59% of the etanercept ± MTX treated patients showed an ACR20 response at Week 12. Indeed, in our register-based study the proportion of responders was also slightly higher for infliximab, the dosage of which was often lower than that used in most trials (5 mg/kg)[5,19]. A dose of 3 mg/kg was sufficient for significant improvement in an open, nonrandomized study[20]. The number of concomitant DMARD and use of MTX and oral corticosteroids were not statistically associated with the response rates in the present study. Moreover, use of DMARD and NSAID as well as corticosteroid dosage decreased during the followup. However, the open aspect of the routine care setting as well as the individually tailored, flexible treatment schemes may affect the likelihood of response favorably. The per-protocol type of analysis used in the present study, i.e., in which dropouts are disregarded, may be another factor leading to higher response rates, especially later in the followup (12 and 24 months), compared with an intent-to-treat approach.

The proportions of patients using concomitant NSAID and MTX were largely in accord with earlier observations[5,6,7,21], while use of oral corticosteroid and DMARD per se was more frequent in the present cohort of patients. However, use of oral corticosteroid was less common in this cohort (40%) compared to patients with RA, of whom around 85% use oral corticosteroid at baseline according to ROB-FIN data. The relatively high frequency of corticosteroid use in the patients with PsA presumably relates to the

Table 2. Use of concomitant disease-modifying antirheumatic drugs (DMARD) and oral corticosteroid at commencement of infliximab and etanercept therapy.

	Infliximab, n = 38		Etanercept, n = 75	
	%	Dose*, median (range)	%	Dose*, median (range)
No. DMARD (± oral corticosteroid)				
0	8		21	
1	53		48	
2	26		31	
3	13		0	
Methotrexate	71	13.75 mg/wk (5–25)	44	15 mg/wk (8.75–25)
Sulfasalazine	26	2 g (1–3)	15	2 g (1–3)
Cyclosporine	8	100 (75–150)	20	150 (50–350)
Leflunomide	5	15 (10–20)	13	20 (10–20)
Sodium aurothiomalate**	18	16.7 mg/wk (10–25)	1	12.5 mg/wk (range NA, n = 1)
Hydroxychloroquine	8	300 (—)	5	300 (—)
Podophyllotoxin derivative	5	300 (—)	8	300 (200–300)
Azathioprine	3	75 (range NA, n = 1)	1	100 (range NA, n = 1)
Auranofin	0	—	1	6 (range NA, n = 1)
Oral corticosteroid	53	7.5 (2.5–15)	29	5 (2.5–15)

* Daily dose in milligrams unless otherwise indicated. ** Dose calculated per week due to differing administration schedules. NA: not applicable.

Table 3. Percentages of patients receiving etanercept using disease-modifying antirheumatic drugs (DMARD) and nonsteroidal antiinflammatory drugs (NSAID), at various times during 24 months of followup.

	Baseline	3 Months	12 Months	24 Months
No. concomitant DMARD				
0	21	20	35	33
1	48	67	60	61
2	31	14	6	6
3	0	0	0	0
NSAID use				
Continuously	47	14	17	12
Temporarily as needed	39	59	50	55
Not used	15	28	33	33

combination treatment strategy commonly used in treatment of RA in Finland, and which seems to be applied for PsA patients with active peripheral arthritis. The common usage of MTX in the treatment of PsA in clinical practice[14,22,23], despite the limited evidence of effectiveness in this indication[4,24], has been based on practical experience and due partly to a lack of other options. In the present study, MTX was most frequently used by patients taking infliximab, possibly reflecting a concern for development of human antichimeric antibody (HACA), or the higher baseline disease activity in this group. This would be compatible with the finding that use of oral corticosteroid was also more frequent in this group. The more frequent usage of other DMARD, compared to that in RCT, may be a reflection, first, of the "saw-tooth" strategy, with conventional DMARD being applied prior to biological therapy on a per-patient basis, similar to therapy in RA; and second, of no requirement for discontinuation of DMARD prior to commencement of the biological drug.

The ACR20 response percentages for infliximab and etanercept at 3 months were of similar magnitude, whereas the ACR50 response percentage was slightly higher for infliximab (not statistically significant). During the followup, response percentages for infliximab tended to decrease, whereas the percentages for etanercept tended to increase, so that the percentages were somewhat higher for etanercept at 12 and 24 months (not statistically significant). One possible explanation for the decrease in response percentages of infliximab could be the development of HACA, which affected 4.5% of PsA patients by 22 weeks of therapy and 15.4% by 66 weeks in the IMPACT 2 trial[5,25], and nearly half of RA patients within 1 year in an open, prospective observational study[26]. This difference may be explained by the lower dosage of infliximab in the latter study (5 mg/kg vs 3 mg/kg), and may therefore be relevant also in the present register-based study.

ACR50 response has been associated with cost-effective anti-TNF treatment in RA[13], but this remains to be con-

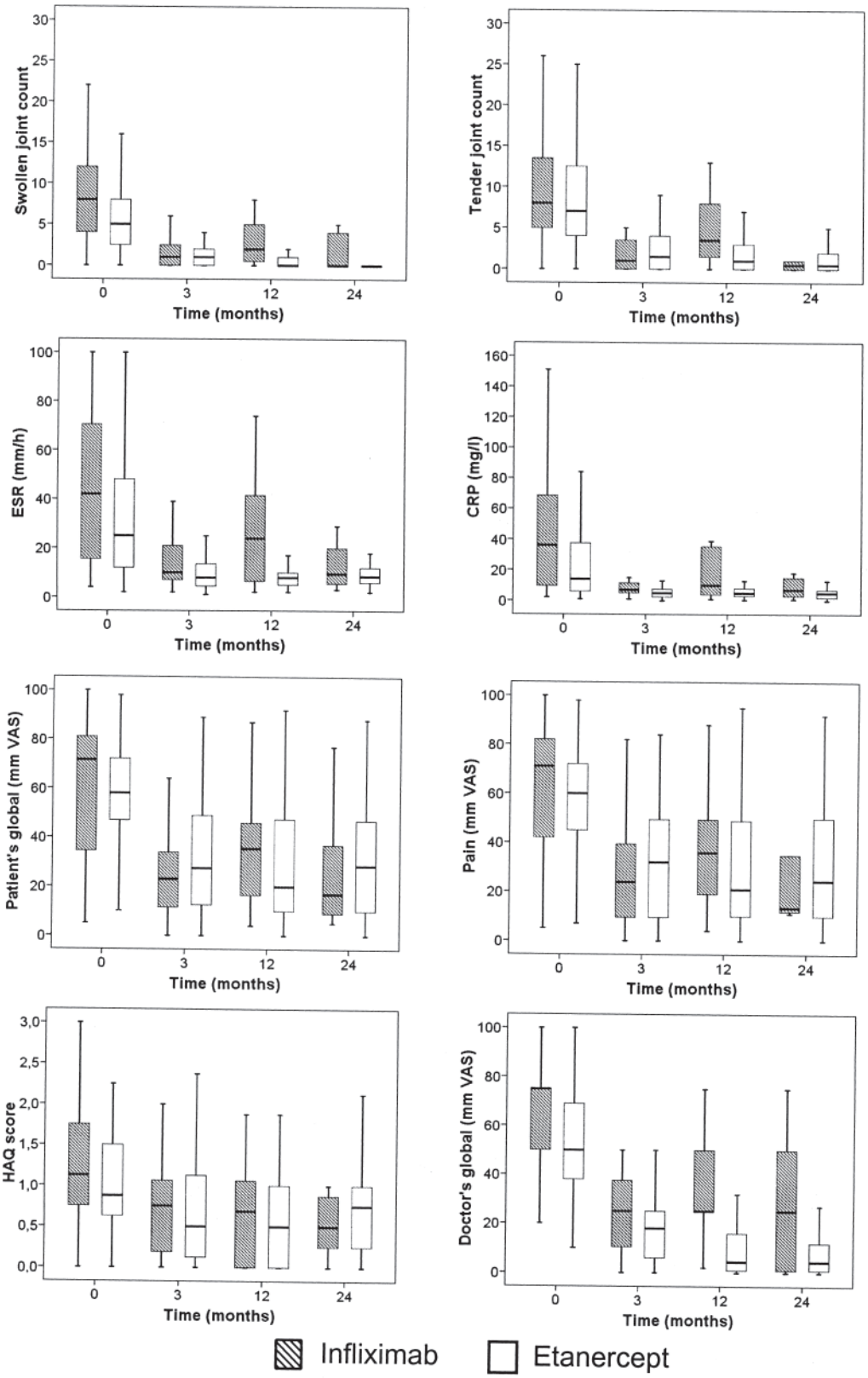

Figure 2. Individual disease measures (swollen joints, tender joints, patient's global assessment, doctor's global assessment, pain, ESR, CRP, HAQ score) of patients with PsA at various times up to 24 months after commencement of infliximab or etanercept. Horizontal line represents the median; the box encloses the middle half of the sample, i.e., the interquartile range. Whiskers extend to the minimum and maximum values, excluding extreme values. Extreme values have been omitted in all graphs for clarity.

firmed for PsA. However, based on the ROB-FIN data, ACR50 responses for PsA were in the same range as those seen in RA.

Our study suffers from 2 limitations, namely, (1) that the distal interphalangeal joints are not included in the 54 swollen joint and 53 tender joint indices used in ROB-FIN; and (2) that sufficient data on axial and enthesitic involvement were not available for this cohort of patients, while data on skin and nail involvement were not specifically collected. One can conclude, however, that peripheral arthritis was an essential feature of our cohort, as 81% had polyarthritis (≥ 5 swollen and/or tender joints) and 15% had oligoarthritis (2 to 4 swollen and/or tender joints), according to the 54 swollen joint and 53 tender joint indices at baseline.

Anti-TNF-α therapy, in this study often used in combination with conventional DMARD, appeared to have limited toxicity and persistent effectiveness up to 2 years in patients with severe peripheral PsA.

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REFERENCES

1. Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64 Suppl 2:ii14-ii17.
2. Salaffi F, Carotti M, Gasparini S, Intorcia M, Grassi W. The health-related quality of life in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a comparison with a selected sample of healthy people. Health Qual Life Outcomes 2009;18:7-25.
3. Ravindran V, Scott DL, Choy EH. A systematic review and meta-analysis of efficacy and toxicity of disease modifying anti-rheumatic drugs and biological agents for psoriatic arthritis. Ann Rheum Dis 2008;67:855-9.
4. Pipitone N, Kingsley GH, Manzo A, Scott DL, Pitzalis C. Current concepts and new developments in the treatment of psoriatic arthritis. Rheumatology 2003;42:1138-48.
5. Antoni C, Krueger GG, de Vlam K, Birbara C, Beutler A, Guzzo C, et al. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis 2005;64:1150-7.
6. Mease PJ, Goffe BS, Metz J, VanderStoep A, Finck B, Burge DJ. Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial. Lancet 2000;356:385-90.
7. Mease PJ, Kivitz AJ, Burch FX, Siegel EL, Cohen SB, Ory P, et al. Etanercept treatment of psoriatic arthritis: safety, efficacy, and effect on disease progression. Arthritis Rheum 2004;50:2264-72.
8. Mease PJ, Gladman DD, Ritchlin CT, Ruderman EM, Steinfeld SD, Choy EH, et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. Arthritis Rheum 2005;52:3279-89.
9. Nordström DC, Konttinen L, Korpela M, Tiippana-Kinnunen T, Eklund K, Forsberg S, et al. Classic disease modifying anti-rheumatic drugs (DMARDs) in combination with infliximab. The Finnish experience. Rheumatol Int 2006;26:741-8.
10. Konttinen L, Honkanen V, Uotila T, Pöllänen J, Waahtera M, Romu M, et al. Biological treatment in rheumatic diseases: results from a longitudinal surveillance: adverse events. Rheumatol Int 2006;26:916-22.
11. Konttinen L, Kankaanpää E, Luosujärvi R, Blåfield H, Vuori K, Hakala M, et al. Effectiveness of anakinra in rheumatic disease in patients naive to biological drugs or previously on TNF blocking drugs: an observational study. Clin Rheumatol 2006;25:882-4.
12. Konttinen L, Tuompo R, Uusitalo T, Luosujärvi R, Laiho K, Lähteenmäki J, et al. Anti-TNF therapy in the treatment of ankylosing spondylitis: the Finnish experience; ROB-FIN Study Group. Clin Rheumatol 2007;26:1693-700.
13. Virkki LM, Konttinen YT, Peltomaa R, Suontama K, Saario R, Immonen K, et al. Cost-effectiveness of infliximab in the treatment of rheumatoid arthritis in clinical practice. Clin Exp Rheumatol 2008;26:1059-66.
14. Kyle S, Chandler D, Griffiths CE, Helliwell P, Lewis J, McInnes I, et al. Guideline for anti-TNF-α therapy in psoriatic arthritis. Rheumatology 2005;44:390-7.
15. Gottlieb A, Korman NJ, Gordon KB, Feldman SR, Lebwohl M, Koo JY, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol 2008;58:851-64.
16. 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.
17. Karvonen S-L, Cajanus S, Hannuksela-Svahn A, Heikkilä E, Höök-Nikanne J, Koulu L, et al. The diagnosis and treatment of psoriasis and psoriatic arthritis [Finnish]. Current Care guideline 2007. [Internet. Accessed June 22, 2010.] Available from: www.kaypahoito.fi
18. Hakala M, Hannonen P, Helve T, Korpela M, Kunnamo I, Möttönen T, et al. Rheumatoid arthritis. Current Care guideline 2003 (updated 2009). [Internet. Accessed June 22, 2010.] Available from: www.kaypahoito.fi
19. Antoni CE, Kavanaugh A, van der Heijde D, Beutler A, Keenan G, Zhou B, et al. Two-year efficacy and safety of infliximab treatment in patients with active psoriatic arthritis: findings of the Infliximab Multinational Psoriatic Arthritis Controlled Trial (IMPACT). J Rheumatol 2008;35:869-76.
20. Salvarani C, Cantini F, Olivieri I, Macchioni P, Padula A, Niccoli L, et al. Efficacy of infliximab in resistant psoriatic arthritis. Arthritis Rheum 2003;49:541-5.
21. Williamson L, Dockerty JL, Dalbeth N. Treatment of psoriatic arthritis. Rheumatology 2004;43:938-9.
22. Taylor WJ, Korendowych E, Nash P, Helliwell PS, Choy E, Krueger GG, et al. Drug use and toxicity in psoriatic disease: focus on methotrexate. J Rheumatol 2008;35:1454-7.
23. Marguerie L, Flipo RM, Grardel B, Beaurain D, Duquesnoy B, Delcambre B. Use of disease-modifying antirheumatic drugs in patients with psoriatic arthritis. Joint Bone Spine 2002;69:275-81.
24. Willkens RF, Williams HJ, Ward JR, Egger MJ, Reading JC, Clements PJ, et al. Randomized, double-blind, placebo controlled trial of low-dose pulse methotrexate in psoriatic arthritis. Arthritis Rheum 1984;27:376-81.
25. Kavanaugh A, Krueger GG, Beutler A, Guzzo C, Zhou B, Dooley LT, et al. Infliximab maintains a high degree of clinical response in patients with active psoriatic arthritis through 1 year of treatment: results from the IMPACT 2 trial. Ann Rheum Dis 2007;66:498-505.
26. Wolbink GJ, Vis M, Lems W, Voskuyl AE, de Groot E, Nurmohamed MT, et al. Development of antiinfliximab antibodies and relationship to clinical response in patients with rheumatoid arthritis. Arthritis Rheum 2006;54:711-5.