

BIOREPORTAP, AN ELECTRONIC CLINICAL RECORD COUPLED WITH A DATABASE: AN EXAMPLE OF ITS USE IN A SINGLE CENTRE

Campanilho-Marques R^{*†}, Polido-Pereira J^{**†}, Rodrigues A^{*}, Ramos F^{*}, Saavedra MJ^{*}, Costa M^{*}, Martins F^{***}, Pereira da Silva JA^{*}, Canhão H^{**}, Fonseca JE^{**}

Abstract

Aims: To evaluate the efficacy and safety of the treatment of psoriatic arthritis (PsA) patients with tumor necrosis factor (TNF) antagonists in the Rheumatology Department of Hospital de Santa Maria using the BioReportAP.

Methods: The Portuguese Society of Rheumatology (SPR) developed an electronic medical chart coupled with a database for the follow up of PsA patients, the BioReportAP, which was launched in May 2009. This evaluation was based on all the PsA patients that were on active treatment with TNF antagonists in September 2009 and were registered in the BioReportAP. All the previous data on these patients were introduced in BioReportAP using the prospective paper based follow up protocol that this Department was using since 1999. Only patients with more than 9 months of treatment were analyzed.

Results: Forty-two patients with PsA, actively treated with anti-TNF agents in September 2009, for at least 9 months, were analyzed in BioReportAP. Twenty-three patients were male (55%) and nineteen were female (45%). The average age of these patients was 49.8±10.9 years old, the average disease duration was of 10.7±5.6 years and the mean duration of biological therapy was of 37.8±27.8 months. For the 81% of patients with peripheral joint disease there was a mean reduction of more than 80% in the swollen and tender joint counts, and almost 50% in the health assessment questionnaire (HAQ) value. In the 19% of the patients with

axial involvement the reduction of BASDAI and BASFI was not statistically significative. On top of that, PASI score suffered a reduction of 64%. Fourteen patients (33.3%) had to switch their TNF antagonist treatment. 58.8% of the switches were due to adverse effects and 41.2% due to therapy failure. Regarding the 56 adverse reactions registered, only one was a severe reaction. The remaining adverse reactions were not severe and 67% of them were due to infections.

Discussion: The results of this first report of the use of the BioReportAP in clinical practice confirm the efficacy and safety of TNF antagonist treatment in PsA. The results shown here elucidate the potential applications of BioReportAP as a tool for efficacy and safety assessment of PsA patients treated with biotechnological drugs.

Keywords: Psoriatic Arthritis; Registry; BioReportAP; Biological Therapy; Portugal.

Introduction

Psoriatic arthritis (PsA) has been defined as an inflammatory arthritis associated with psoriasis and seronegative for rheumatoid factor. PsA affects men and women almost equally. The average age at onset in most studies is 36-40 years. The classic description of PsA includes five clinical patterns¹. These patterns include distal interphalangeal (DIP) joint involvement, oligoarticular pattern (<5 joints involved) which is usually asymmetric in distribution, a polyarticular pattern (>5 joints involved), which is symmetric in only half the patients, arthritis *mutilans*, which is a very destructive form of arthritis and spondyloarthritis, affecting the sacroiliac joints and the apophyseal joints of the spine, with a clinical pattern often similar to ankylosing spondylitis (AS)².

Over the past few years, there has been a rene-

*Serviço de Reumatologia e Doenças Ósseas Metabólicas, Centro Hospitalar Lisboa Norte – Hospital de Santa Maria

**Unidade de Investigação em Reumatologia, Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa e Serviço de Reumatologia e Doenças Ósseas Metabólicas, Centro Hospitalar Lisboa Norte – Hospital de Santa Maria

***Sociedade Portuguesa de Reumatologia

[†]Both author contributed equally to this work

wed interest in the treatment of PsA. This has resulted from the advent of tumor necrosis factor (TNF) antagonist therapy that had proven to be highly effective in both psoriasis and PsA³. TNF is a leading cytokine for the inflammatory aspects noted in the skin and joints and it is a key upstream factor in the activation of other chemokines and cytokines, which may lead to cartilage and bone destruction and to skin scarring. Thus, it is not surprising that tackling TNF leads to marked improvement in joint and skin symptoms and prevents joint destruction and permanent skin lesions. At this moment, only 3 anti TNF treatments are reimbursed in Portugal for the treatment of adult patients with active PsA who have responded inadequately to disease-modifying anti-rheumatic drugs (DMARDs): adalimumab, etanercept and infliximab. Etanercept, a recombinant human soluble TNF receptor is a dimeric fusion protein consisting of the extracellular portion of the human p75 TNF receptor linked to the Fc portion of a Type 1 human immunoglobulin (IgG1). The primary action of etanercept is to bind and inactivate soluble and cell-bound TNF and lymphotoxin alpha. In adults, it is administered 25 mg twice a week or 50 mg once a week. Infliximab is a chimeric monoclonal antibody that binds specifically to human TNF and is composed of human constant and murine variable regions. Infliximab is administered as an intravenous infusion, at a dose of 5 mg/Kg, at 0, 2, and 6 weeks followed by infusions every 8 weeks. Adalimumab is a fully human anti-TNF IgG1 antibody, with a mechanism of action similar to infliximab. It is administered as a subcutaneous injection at a dose of 40 mg every two weeks.

In order to measure disease activity, progression and change with therapy in PsA patients, it is important to use accurate, reliable and feasible outcome measures that can ideally be employed in longitudinal cohorts, clinical trials and clinical practice^{4,5}.

Until recently, there has been a low investment on the development of this kind of methodology applied to PsA. With emerging therapies, the focus on the methodology of outcome assessment has increased to ensure that discriminative instruments are used. Most tools applied to the quantification of PsA outcomes have been borrowed from rheumatoid arthritis (RA) and ankylosing spondylitis (AS) outcome studies, but some have been specifically tested in PsA³. However, the relative variability of PsA clinical manifestations still poses a

great challenge in the assessment of real life cohorts, which were not selected through complex inclusion and exclusion criteria, as is the case of clinical trials.

A key assessment in rheumatology clinical trials is the counting of the number of tender and swollen joints in a patient. Variable numbers of joints are counted in various systems, such as the American College of Rheumatology (ACR) joint count of 68 tender and 66 swollen (excluding the hips from assessment of swelling), developed in 1949 for the evaluation of RA⁶. This has been frequently adapted to be used for the evaluation of PsA patients with peripheral joint involvement (without axial skeleton involvement) – the so called “RA like” patients. These joint counts are then combined with other core measures of disease activity (also adapted to the use in PsA), such as patient and physician assessed global health, through the use of a 100 mm visual analogue scale (VAS), pain (also using a VAS) and inflammation markers (Erythrocyte Sedimentation Rate, ESR, and C reactive protein, CRP)⁷. Another classical RA activity measurement, the DAS 28 (disease activity score, based on 28 swollen and tender joints, ESR and patient global health VAS) has been also frequently used in PsA⁸.

The ASessment in Ankylosing Spondylitis (ASAS) working group has recommended the use of a number of outcome measures for spinal involvement in AS, which includes the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)⁹, the Bath Ankylosing Spondylitis Function Index (BASFI)¹⁰ and a set of mobility measures. These measurements have been used to evaluate PsA in patients that have axial skeleton involvement – “AS like” patients.

PsA joint disease activity is commonly not mirrored by skin disease. It thus seems logical to assess skin disease separately. The most widely used system is the Psoriatic Area Severity Index (PASI)^{11,12} and this has been introduced in the description of PsA clinical cohorts.

Physical function refers to the abilities or difficulties in daily activities such as walking, opening jars, playing sports, lifting heavy objects, writing and so forth. Assessing physical function by self-reported questionnaire has become a favored approach because no special equipment or testing personnel is required. The Health Assessment Questionnaire (HAQ)¹³ is a validated questionnaire for measuring physical function in RA. Because

PsA may affect people in a way similar to RA it has been considered reasonable to use such measure in PsA.

An important aspect of the evaluation of the results of DMARDs treatment is the repercussion on structural joint damage. Radiologic signs of joint damage remain the standard method in RA clinical trials, despite the advent of newer modalities such as ultrasound and magnetic resonance imaging (MRI). In PsA the distribution of joint disease is not predictable and it remains to be determined which joints should be scored to get a sufficiently valid measurement of joint damage.

Simple measures of inflammation, such as the acute phase reactants, which include ESR and CRP are used, but are not reliably elevated in patients with PsA, even with active inflammation. Desirable but not essential symptom domains to measure include enthesitis, dactylitis, nails and fatigue¹⁴⁻¹⁶.

As has already been done for RA and AS, the Portuguese Society of Rheumatology (SPR) has developed an informatics platform which combines features of electronic clinical chart with a database for PsA patients who are being treated with biotechnological drugs – BioReportAP. This article is the first application of the use of BioReportAP to a cohort of PsA patients being followed in a Portuguese Rheumatology Department. In addition, this is also the first report of a Portuguese cohort of PsA patients treated with TNF antagonists. In fact, SPR has promoted 2 national reports on the use of biotechnological drugs in RA¹⁷ and AS¹⁸ but there is no report on patients with PsA. Moreover, despite the existence of national guidelines for treatment of RA¹⁹ and AS²⁰ patients with biotechnological DMARDs, SPR has not developed this instrument for PsA, which means that the results of this paper can be taken into account in the future elaboration of such guidelines. BioReportAP will be an important tool for monitoring the efficacy and safety of the use of TNF antagonists in PsA at a national level and this first practical application will help to detail the mechanisms for recording and analysis of data.

Material and methods

BioReportAP is an electronic clinical chart that is linked to a database, built on the Plataforma.NET (VB.NET) and the SQL DatabaseServer. The NET Plataforma (Microsoft) allows the development of

software applications for Windows, based on VB.NET programming language to build all the screens used. The information entered is stored in the SQL server database management system (Microsoft).

BioReportAP was launched on 2 May 2009 at a national level by SPR and all PsA patients treated with biologic therapies in the Rheumatology Department of Santa Maria's Hospital are being collected prospectively from that date. In addition, this department had also previously started (since 1999) a prospective evaluation of all rheumatic patients treated with biotechnological drugs structured on a paper based protocol. This protocol has been adapted from an initial version prepared for RA patients published initially in 2001 and updated recently²¹. This evaluation was based on all PsA patients that were on active treatment with TNF antagonists in September 2009 for more than 9 months and were registered in the BioReportAP. The criteria for starting TNF antagonists was based on the clinical opinion of the assisting physician reflecting, however, the Portuguese recommendations for starting biotechnological drugs in RA¹⁹ and AS²⁰ patients were also taken into account.

The key variables included in the BioReportAP were: sex, age, birthplace, education, current employment status, prior disease, personal history, general clinical data (type of arthritis, the onset of symptoms and date of diagnosis, radiological signs, HLA B27 typing, body mass index, smoking and alcohol consumption), surgeries, prior therapy (DMARD) and current therapy (name of the drug, starting date, dose, consumption of NSAIDs and corticosteroids) and adverse effects. Severe adverse reactions were defined as the occurrence of death, hospitalization or any event that causes permanent damages. The tuberculin skin test (TST), chest x-ray results, tuberculosis risk factors and latent tuberculosis treatment is also recorded. The complete joint count is registered, as well as patient and physician's global health VAS, patient's pain VAS, HAQ and inflammation markers (ESR and CRP). A computer assisted automatic DAS 28 calculation is available (including CRP or ESR and 3 or 4 variables)^{7,8}. For patients with axial involvement BASDAI, BASFI and mobility measurements as defined by the ASAS group are used. Psoriasis Area and Severity Index (PASI) is the score used for skin involvement.

Results

Forty-two patients with PsA, who in September 2009 were under treatment with anti-TNF agents, for at least 9 months, were registered in BioRePortAP and analyzed. Twenty-three patients were male (55%) and nineteen were female (45%). The average age of these patients was 49.8 ± 10.9 years old. The youngest was 38 and the eldest was 60 years old. The average age at diagnosis was 38.1 ± 11.6 years old and the average disease duration at the current evaluation was of 10.7 ± 5.6 years. The shortest disease duration was of 5 years and the longest disease duration was of 16 years. The mean disease duration at the beginning of the biological treatment was of 7.9 ± 6.5 years and the mean duration of biological therapy currently under way was of 37.8 ± 27.8 months (minimum of 10 months and maximum of 5 years).

For a total of 42 patients 19% had axial skeleton involvement and 81% peripheral joint involvement. HLA-B27 was registered in 24 patients and was positive in 4 (16.7%) of them.

Due to the high risk of tuberculosis in patients with inflammatory joint diseases treated with anti-TNF drugs, the tuberculin skin test (TST) with two units of RT23 and chest x-ray were performed before starting therapy. For further evaluation 14 patients (33.3%) were referred to specialized tuberculosis centers (Centros de Diagnóstico Pneumológico, CDP) and eleven patients (26.2%) received latent tuberculosis treatment. Tuberculin skin test was performed in all patients prior to starting anti TNF treatment but in two of them there was no registry of the result. Six of the 27 patients with TST < 5mm repeated the test and in all of them the result was less than 5mm. In none of them was prescribed prophylactic therapeutic but 4 of the 24 patients with initial TST < 5mm and normal chest X-ray were submitted to isoniazid treatment due to the presence of epidemiological risk factors for tuberculosis

(in 2 isoniazid 300mg/day during 6 months was prescribed and in the other 2 it was taken during 9 months). In 5 of the 8 patients with TST 5-10mm isoniazid (300mg/day during 6 months in 4 patients and during 9 months in 1) was prescribed due to the presence of prior immunosuppressive treatment. All the 5 patients with TST > 10mm received latent tuberculosis treatment: 3 were treated with isoniazid 300mg/day during 9 months, 1 received isoniazid 300mg/day during 6 months and 1 isoniazid and rifampicin during 3 months.

At the time of the current evaluation, in a total of 42 patients, 18 were under treatment with etanercept (42.9%), 16 with infliximab (38.1%) and 8 with adalimumab (19%). Only 26.2% were on monotherapy with anti-TNF drugs and the majority (73.8%) was being treated with an associated conventional DMARD. In 18 patients treated with etanercept, only 5 (27.8%) were on monotherapy and most (55.5%) were being treated concomitantly with methotrexate (MTX). For the 16 patients being treated with infliximab only 37.5% were on monotherapy and 57.3% have associated MTX or other DMARDs. All of the adalimumab treated patients were receiving concomitant MTX (Table I).

Fourteen patients (33.3%) had to switch their TNF antagonist treatment and 3 of them made two switches, so in total there were 17 switches. 58.8% of the switches were due to adverse effects and 41.2% due to therapy failure (Table II).

To evaluate the 81% of patients with predominant peripheral joint involvement the 68 joint counts and the DAS28 score were applied. The average initial (at the beginning of biologic therapy) number of tender joints (68 joint count) was 16.3 ± 10.4 and the final (at the moment of evaluation) was 3 ± 5.1 ($p=0.00005$). The swollen joint (68 joint count) count at the beginning of treatment was 9.4 ± 9.7 and at the final evaluation was 1.2 ± 2.6 ($p=0.0000659$) (Figure 1). The initial DAS28 was 3.6 ± 2.6 and the final was 3 ± 1.6 ($p=0.140$) (Figure 2).

Table I. Biological therapy and DMARDs

	Monotherapy	MTX	SLZ	MTX/PDN	MTX/PDN/SLZ	PDN	TOTAL
Infliximab	37.5	12.5	6.25	31.25	12.5	0	100
Etanercept	27.8	44.4	5.6	11.1	0	11.1	100
Adalimumab	0	62.5	0	25	12.5	0	100

Number of DMARDs (percentages) currently in use in association with biological therapy (anti-TNF) on Psoriatic Arthritis patients
MTX: Methotrexate; SLZ: Sulphasalazine; PDN: Prednisone

Table II. Switch between biological therapies

Previous therapy	Current therapy	Number of patients	Reason for Switch	
			Adverse effects	Therapeutic failure
Etanercept (8)	Infliximab	6	Pancreatitis – 1 Injection site reaction – 2	3
	Adalimumab	2	Injection site reaction – 2	0
Infliximab (7)	Etanercept	3	Injections site reaction – 1 Upper respiratory infection – 1	1
	Adalimumab	4	Injection site reaction – 2 Transaminitis – 1	1
Adalimumab (2)	Infliximab	1	0	1
	Etanercept	1	0	1

Number and reason for switches (in absolute numbers)

For the 19% of PsA patients with spinal involvement – “AS like patients” BASDAI and BASFI were used. The average initial BASDAI was 4.3 ± 2.9 and the final was 3.4 ± 1.9 ($p=0.263$). The average initial BASFI was 4.7 ± 1.6 and the final was 4.3 ± 1.9 ($p=0.386$) (Figure 3 and 4).

Concerning the acute phase reactants, the initial ESR was 25.9 ± 21.9 mm/1st hour and the final was 19.1 ± 21.5 mm/1st hour ($p=0.084$). The initial CRP was 2.1 ± 3.7 mg/dL and the final 0.9 ± 1.8 mg/dL ($p=0.04$).

To assess skin disease in PsA the PASI was used. The mean initial PASI was 6.3 ± 13.5 and the final was 2.2 ± 5.5 ($p=0,056$) (Figure 5). In 40.5% of patients there was a reduction of at least 50% of the PASI value.

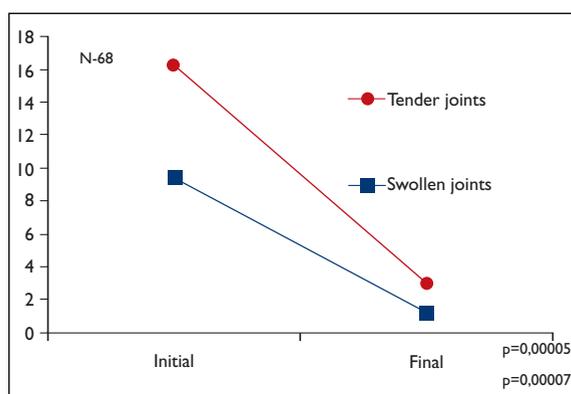


Figure 1. Number of tender and swollen joints initial and final (at the moment of the last evaluation) of the 81% of patients with peripheral involvement (mean follow-up – 37.8 ± 27.8 months).

To assess physical function the self-reported questionnaire HAQ was used. The initial HAQ was 1.5 ± 1 and the final was 0.7 ± 0.8 ($p=0.0002$).

At the end of the evaluation period, 28.6% of the peripheral joints affected patients had a DAS28 superior to 3.2, 12.5% of the axial involved patients had a BASDAI superior to 40 and 60% improved less than 50% in their skin condition.

The only documented severe adverse reaction was due to a case of pancreatitis, which was considered by the assisting physician to be unlikely related to the use of TNF antagonists. In 23.8% of the mild adverse reactions, the drug had to be discontinued definitely and switched to another TNF antagonist, while in the remaining patients a temporary drug withhold proved to be enough. No tuberculosis case was registered. According to the exposure time, 1.3 serious adverse reactions occurred by 100 patient-year (Figure 6).

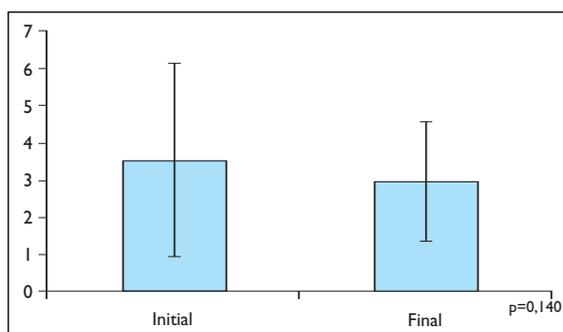


Figure 2. Value of DAS 28 (Disease Activity Score) initial and final (at the moment of the last evaluation) of the 81% of patients with peripheral involvement (mean follow-up – 37.8 ± 27.8 months).

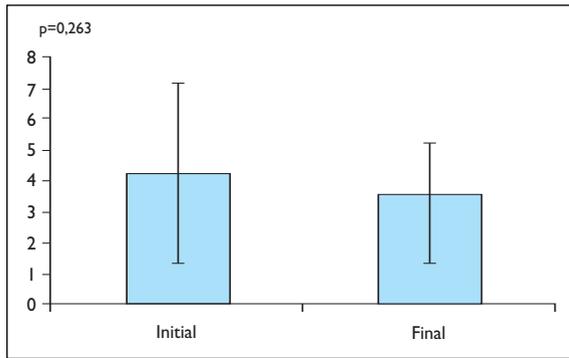


Figure 3. Bath Ankylosing Spondylitis Disease Activity Index initial and final (at the moment of the last evaluation) of the 19% of patients with axial involvement (mean follow-up - 37.8±27.8 months).

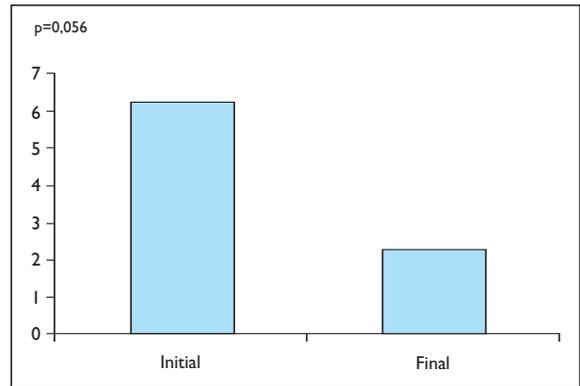


Figure 5. Psoriatic Area and Severity Index (PASI) initial and final (at the moment of the last evaluation) in all the patients (mean follow-up - 37.8±27.8 months).

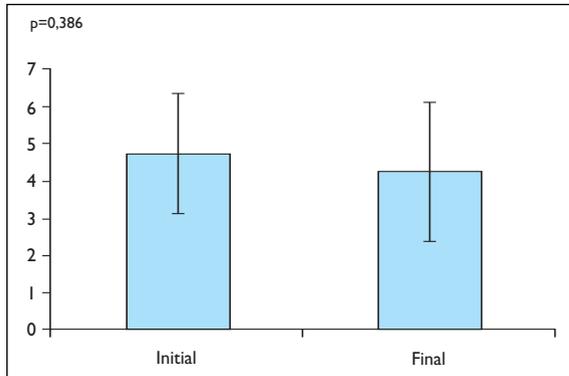


Figure 4. Bath Ankylosing Spondylitis Functional Index initial and final (at the moment of the last evaluation) of the 19% of patients with axial involvement (mean follow-up - 37.8±27.8 months).

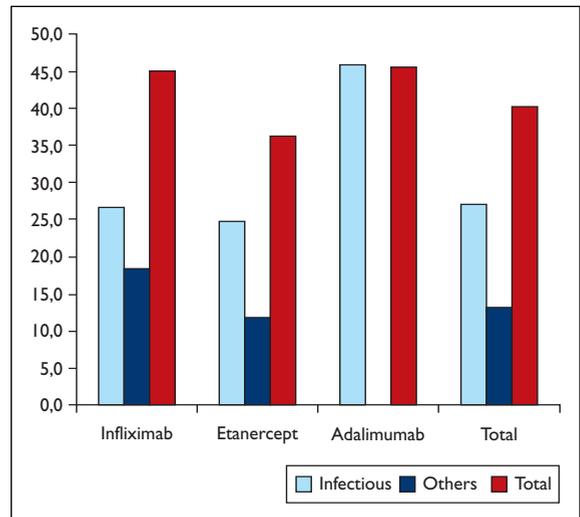


Figure 6. Number of adverse reactions per 100 patient-years.

Discussion

The results of this first report of the use of the BioRePortAP in clinical practice confirm the efficacy and safety of TNF antagonist treatment in PsA. In fact, in a cohort of 42 patients, with a mean treatment duration of 37.8±27.8 months (minimum exposure to the drug of 9 months) in the patients with peripheral joint disease there was a mean reduction of more than 80% in the swollen and tender joint counts and in those with an axial involvement there was a mean reduction in the BASDAI score of 34%. On top of that, the mean PASI score suffered a reduction of 64%. On the other hand, in this group of patients there was a low rate of serious adverse effects, although a relatively high number of mild adverse effects were reported.

The impact on functional scores, such as BASFI

(mean reduction of 0.5) and HAQ (mean reduction of 0.9), reflects the relatively long disease duration that these patients had at the time of starting these drugs. However, this disease duration (slightly less than 8 years) is lower than the one that was verified in the previous RA (almost 12 years) and AS (almost 14 years) Portuguese cohorts of patients treated with biotechnology drugs^{17,18}.

Fourteen patients (33.3%) had to switch from one TNF antagonist to another one due to lack of efficacy in 41.2% of the cases. Three of these patients had to switch again to a third anti TNF drug also due to lack of efficacy. The remaining causes for switching were adverse effects. Even with additional measures to ensure the effectiveness of treat-

ment such as switching and associating DMARDs (73.8% of the patients) there were 28.6% of the peripheral affected patients with a DAS28 superior to 3.2, 12.5% of the axial involved patients with a BASDAI superior to 40 and 60% improved less than 50% in their skin condition. Moreover, the improvements observed in mean DAS28 and mean BASDAI scores were not statistically significant. These observations suggest that some of these patients should be reassessed for treatment optimization (classical DMARD readjustment, switch to another TNF antagonist and review of the treatment options for skin disease).

The dissociation between the reduction in the 68 joint count and the results of the DAS28 score suggest that DAS28 is a weak discriminating assessment tool for PsA.

Due to the high incidence of tuberculosis in the general Portuguese population, particularly in inflammatory joints diseases treated with anti-TNF drugs, strict recommendations for the diagnosis and treatment of latent tuberculosis infection were elaborated by the Portuguese Society of Rheumatology²². Since 2002, specific guidelines for screening candidates to anti-TNF therapy for active and latent TB have been followed. The first version of these guidelines was published in September 2006 and placed on the General Directorate of Health Internet website in December 2006²³. Before this date, the threshold of TST positivity was higher (TST>10mm) and that explains why 3 of the patients, who had TST between 5 and 10mm and started biological therapy before 2002 didn't receive latent tuberculosis infection treatment. In the recent Portuguese recommendations the TST is considered positive if: ≥ 5 mm in any patient who is about to start anti-TNF treatment and is concomitantly immunosuppressed (prednisolone in doses higher than 10 mg/day and/or with immunosuppressant drugs, such as MTX, cyclosporine, azathioprine, leflunomide or cyclophosphamide, regardless of the dose); or ≥ 10 mm in patients who are not taking previous immunosuppressing drugs. Four of the patients had a negative TST but were, also in accordance to these guidelines, submitted to treatment because they were immunosuppressed and had epidemiologic risk factors for tuberculosis. Fourteen of the patients were referred to Centro Diagnóstico Pneumológico (CDP) or to a Pulmonology Department, corresponding to the ones that had started the treatment more recently, following the 2008 updated version of these guideli-

nes that recommend that all patients in evaluation for TNF antagonist therapy should be referred to a tuberculosis specialized centre.

Regarding safety it is important to highlight that several mild infectious adverse effects were detected. However, severe adverse effects were very rare. The way the Day Care Unit of Rheumatology Department of the Hospital de Santa Maria is organized favors the detection of all the complications because patients are advised to seek medical support in the Day Care Unit whenever a complication occurs. On the other hand, this easy contact combined with a low threshold for the diagnosis of infections might contribute to the low rate of severe adverse effects.

The results shown here elucidate the potential applications of BioRePortAP as a tool for efficacy and safety assessment of PsA patients treated with biotechnological drugs. Moreover this informatics tool can also act as a guarantee of good clinical practice and a source of data for self assessment of a Rheumatology department.

The characteristics of this first report of the BioRePortAP, including only a population that was on therapy at a certain date (September 2009), limits the type of conclusions that can be achieved. However, at long term evaluations, BioRePortAP will be able to inform precisely on drug survival, which is the main limitation of the current assessment.

Correspondence to

Raquel Campanilho-Marques
Serviço de Reumatologia e Doenças Ósseas Metabólicas,
Centro Hospitalar Lisboa Norte
Avenida Professor Egas Moniz
1649-035 Lisboa
Tel: +351 966 253 128
E-mail: raquelpcmarques@gmail.com

References

- Glandman DD. Psoriatic arthritis. *Dermatol Ther* 2009; 22: 40-55.
- Taylor WJ. The epidemiology of psoriatic arthritis. *Curr Opin Rheumatol* 2002; 14: 98-103.
- Taylor WJ. Assessment of outcome in psoriatic arthritis. *Curr Opin Rheumatol* 2004; 16: 350-353.
- Mease JP. Spondyloarthritis Update: New insights Regarding Classification, Pathophysiology and management. *Bull NYU Hosp Jt Dis* 2008; 66: 203-209.
- Mease PJ, Antoni CE, Gladman DD et al. Psoriatic arthritis assessment tools in clinical trials. *Ann Rheum Dis* 2005; 64: 49-54.
- Van Gestel AM, Prevoo ML, van 't Hof MA et al. Development and validation of the European League

- Against Rheumatism response criteria for rheumatoid arthritis. *Arthritis Rheum* 1996; 39: 34-40.
7. Deandrade JR. A seven-day variability study of 499 patients with peripheral rheumatoid arthritis. *Arthritis Rheum* 1965; 8: 302-334.
 8. Smolen JS, Breedveld FC, Elberl G et al. Validity and reability of the twenty-eight-joint count for the assessment of rheumatoid arthritis activity. *Arthritis Rheum* 1995; 38: 38-43.
 9. Garrett S, Jenkinson T, Kennedy LG et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994; 21: 2286-2291.
 10. Calin A, Garrett S, Whitelock H et al. New approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol* 1994; 21: 2281-2285.
 11. Frederiksson T. Severe psoriasis – oral therapy with a new retinoid. *Dermatol* 1994; 157: 238-244.
 12. Gottlieb AB. The National Psoriasis Foundation Psoriasis Score (NPF-PS) system versus the Psoriasis Area Severity Index (PASI) and Physician’s Global Assessment (PGA): a comparison. *J Drug Dermatol* 2003; 2: 260:266.
 13. Fries JF, Kraines RG, Spltz Z et al. Measurement of patient outcomes in arthritis. *Arthritis Rheum* 1980; 23: 137-145.
 14. Olivieri I, Cantini F, Salvarani C et al. Fast spin echo-T2-weighted sequences with fat saturation in dactylitis of spondylarthritis. No evidence of enthesal involvement of the flexor digitorum tendons. *Arthritis Rheum* 2002; 46: 2964-2967.
 15. Schentag CT. Validation and normative data for the 0-10 point scale version of the fatigue severity scale (FSS). *Ann Rheum Dis* 2000; 43: 177-181.
 16. McGonagle D, Emery P, Gibbon W et al. Classification of inflammatory arthritis by enthesistis. *Lancet* 1998; 352: 1137-1140.
 17. Grupo de Estudos de Artrite Reumatóide da Sociedade Portuguesa de Reumatologia. Análise de 376 doentes com artrite reumatóide submetidos a terapêutica biológica registados na base de dados de terapêutica biológica da Sociedade Portuguesa de Reumatologia. *Acta Reum Port* 2005; 30: 63-71.
 18. Grupo de Consensos para as terapêuticas biológicas na Espondilite Anquilosante da Sociedade Portuguesa de Reumatologia. Análise de doentes com espondilite anquilosante submetidos a terapêutica biológica registados na base de dados de terapêutica biológica da Sociedade Portuguesa de Reumatologia. *Acta Reum Port* 2005; 30: 253-260.
 19. João Eurico Fonseca, Helena Canhão, Paulo Reis et al. Portuguese guidelines for the use of biological agents in rheumatoid arthritis – March 2010 update. *Acta Reum Port* 2010; 35: 95-98.
 20. Grupo de Consensos para as Terapêuticas biológicas na Espondilite Anquilosante da Sociedade Portuguesa de Reumatologia. Consensos sobre a utilização de antagonistas do TNF na terapêutica da espondilite anquilosante. *Acta Reum Port* 2005; 30: 155-159.
 21. Fonseca JE, Canhão H, Reis P et al. Protocolo de monitorização clínica da artrite reumatóide (PMAR) – revisão de Dezembro de 2007. *Acta Reum Port* 2007 32: 367-374.
 22. Fonseca JE, Lucas H, Canhão H et al. Recommendations for the diagnosis and treatment of latent and active tuberculosis in inflammatory joint diseases candidates for therapy with tumor necrosis factor alpha inhibitors March 2008 update. *Acta Reum Port* 2008; 33: 77-85.
 23. Fonseca JE, Lucas H, Canhão H et al. Recomendações para o diagnóstico e tratamento da tuberculose latente e activa nas doenças inflamatórias articulares candidatas a tratamento com fármacos inibidores do factor de necrose tumoral alfa. *Acta Reum Port* 2006; 31: 237-245.

32nd American Society for Bone and Mineral Research Annual Meeting

Toronto, Canadá
15 a 19 de Outubro 2010