Most Rheumatologists Are Conservative in Active Rheumatoid Arthritis Despite Methotrexate Therapy: Results of the PRISME Survey

ALAIN SARAUX, VALÉRIE DEVAUCHELLE-PENSEC, LUC ENGERRAN, and RENÉ MARC FLIPO

ABSTRACT. ***Objective.*** To evaluate the proportion of patients with rheumatoid arthritis (RA) visiting office-based rheumatologists for persistently active RA despite past or current methotrexate (MTX) treatment, and to describe the management of these patients in France in 2003.

Methods. All French rheumatologists were invited to participate in a cross-sectional postal survey. During a predetermined week, they were to include the first 2 patients seen for RA with a history of past or current MTX treatment. Adequacy of current treatment was assessed based on the 28-joint Disease Activity Score 28 (DAS28) and on current MTX and corticosteroid regimens.

Results. Of the 1800 French rheumatologists, 492 returned 838 assessable patient questionnaires. Mean patient age was 58 years and mean time since RA diagnosis was 10 years; 77% of patients were currently taking MTX, and 51% a corticosteroid. High dosages were noted for MTX (> 15 mg/week) in 20% of patients and for corticosteroid therapy (> 10 mg/day) in 5%. Nevertheless, 41% of patients had active RA (DAS28 score 3.2 to 5.1) and 7% had very active RA (DAS28 score > 5.1). The treatment was left unchanged in 78% of patients, and biological therapy was contemplated in only 16% of patients.

Conclusion. Although half of MTX-treated patients with RA visiting office-based rheumatologists had active or very active disease, a change in treatment was rarely considered. (First Release June 15 2006; J Rheumatol 2006:33:1258–65)

Key Indexing Terms:
RHEUMATOID ARTHRITIS EPIDEMIOLOGY DISEASE ACTIVITY SCORE
METHOTREXATE BIOLOGICAL THERAPY

Rheumatoid arthritis (RA) is the most common inflammatory joint disease, with a prevalence in France of about 0.3%[1]. RA is a chronic progressive disease responsible for joint destruction and functional impairment. It generates a crushing human and economic burden related to alterations in quality of life, severe disability, loss of work days, cost of treatments including joint replacement surgery, and reduced life expectancy[2]. The current management of RA involves early treatment with disease modifying antirheumatic drugs (DMARD). Low-dose methotrexate (MTX) is considered the DMARD of first choice, given its excellent longterm effectiveness and safety in most patients, as shown by extensive clinical experience[3]. However, not all patients respond optimally to currently available DMARD, including MTX, and although there may be major improvement over the course of a study, many patients still show significant clinical activity[4]. For these patients, much of the improvement in clinical status of RA in a real-world setting might be the result of active strategies to treat RA, especially combinations of corticosteroids (joint injection and/or oral administration) and DMARD[5-7].

The recent introduction of biological agents [i.e., anti-tumor necrosis factor-α (TNF-α) and anti-interleukin 1 (IL-1) agents] has expanded the horizons of RA management. Biological agents have shown substantial efficacy in patients with persistent disease activity despite adequate MTX therapy, demonstrating a remarkable ability to slow disease progression and to prevent irreversible structural joint damage[8]. In France, given the cost and the estimated potential risk of biologics in 2003, anti-TNF were mostly prescribed to patients with persistently active RA despite MTX and/or at least 3 prior attempts with DMARD courses and/or corticosteroids (> 10 mg prednisone per day). In 2005, the Club of Rheumatism and Inflammation of the French Society of Rheumatology recommended anti-TNF after failure of MTX of up to 0.3 mg/kg (maximum 25 mg) in patients with RA with Disease Activity Score 28 (DAS28) > 5.1 or DAS28 ≥ 3.2 despite corticosteroids[9].

The objectives of the PRISME survey, carried out in France in 2003 among office-based rheumatologists, were to evaluate the proportion of RA patients with persistent disease activity despite MTX treatment and to describe management

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practices in this situation, most notably factors leading rheumatologists to consider biological therapy.

MATERIALS AND METHODS

Setting and patients. Our study was a cross-sectional postal survey conducted by the polling organization TNS Sofres among the 1800 office-based or office- and hospital-based rheumatologists in France. Reminder telephone calls were made to 547 selected at random. The rheumatologists were asked to include the first 2 patients who sought advice for RA between the 22nd and the 29th of September 2003 and who met the survey inclusion criteria. These criteria consisted of RA fulfilling at least 4 of the 7 criteria in the 1987 American College of Rheumatology (ACR) set[10], current or previous MTX treatment, and a negative history for biological therapy at any time.

Participating physicians and patient questionnaires. Rheumatologists participating in the survey were asked to complete a physician questionnaire and one patient questionnaire for each included patient. The physician questionnaire had 8 items on physician characteristics, practice setting, number of RA patients seen per week, disease duration in RA patients, and practice regarding MTX and/or biological agent use in RA patients.

Patient medical history and clinical status variables included 30 items specifying patient characteristics, comorbidities, history of RA, variables needed to compute the DAS28[11,12] [i.e., tender and swollen joint counts, erythrocyte sedimentation rate (ESR), and disease activity as assessed by the patient on a visual analog scale (VAS) from 0 to 100], plasma C-reactive protein (CRP) level, extraarticular manifestations (rheumatoid nodules, Sjögren's syndrome, pulmonary disorder, tendinitis, atlanto-axial dislocation, and others), radiographic findings, current and past treatments, treatment changes decided during the visit, and whether biological therapy was considered. An open-ended question allowed rheumatologists to describe the reasons for changing or not changing treatment. Criteria for prescription of biologics were not presented to physicians.

Data analysis. To determine whether our sample of survey respondents was representative, we compared it to data in the national directory of rheumatologists (Cegedim Communication Directe, Boulogne-Billancourt, France). DAS28 values were computed at the time of data analysis. Based on DAS28 score values, we defined 4 categories of disease activity: remission < 2.6[8]; mild activity 2.6–3.2; moderate activity > 3.2–5.1, and marked activity > 5.1[11-17]. Corticosteroid doses were expressed as the prednisone-equivalent in milligrams. To identify inadequacy of current therapy (and therefore potential eligibility of the patient for biological therapy), we used 2 criteria sets: The liberal set: persistent RA activity (DAS28 > 3.2) despite MTX at a high dose (≥ 15 mg/week) or combined with high-dose corticosteroid therapy (> 10 mg/day), requirement for high-dose corticosteroid therapy to achieve mildly active or inactive RA with MTX, and/or untoward reactions to MTX; and the conservative set: active disease defined as DAS28 > 3.2 and/or untoward reactions with MTX after at least 3 prior DMARD courses, or corticosteroid therapy in a dosage > 15 mg/day.

Categorical variables were summarized as percentages of patients with each variable in the relevant patient group. Between-group differences were evaluated using the Z test. For continuous variables, we computed descriptive statistics [mean and standard deviation (SD)]. Where appropriate, between-group differences were compared using the Student t test (provided the size of each group was > 30). All p values < 0.05 were considered statistically significant.

RESULTS

Development of the survey. Of the 1800 rheumatologists who were sent questionnaires, 522 (29%) returned physician questionnaires, of which 30 were not assessable, leaving 492 respondents for the study. In addition, the 492 respondents mailed back 923 completed patient questionnaires, of which 85 were not assessable, either because they arrived after the study deadline or because they gave data on patients who had never received MTX therapy; this left 838 patients for the study.

Characteristics of the survey rheumatologists. Table 1 reports details on the 492 rheumatologists. As compared to the national reference data, the survey sample contained significantly more females, as well as fewer rheumatologists working in the Ile de France region and more rheumatologists working in the western and northeastern regions of France. Half the respondents (51%) worked in office practice only, and half (49%) worked part-time in office practice and part-time in hospitals.

Characteristics of patients with RA seen by survey rheumatologists. The mean number of RA patients seen during the survey week was 5.1 ± 3.1. During the survey week, the respondents saw 2366 RA patients in all, with a mean age of 58 years; 73% of patients were aged 50 years or older. Mean RA duration was 10 years. A past or current history of MTX therapy was noted in 76% of patients and a past history of biological agent therapy in 8% of patients. Among these patients, those fulfilling the inclusion criteria were included in the survey.

Characteristics of the survey sample of RA patients. Among the 838 RA patients included in the survey, 80% were women and 20% men, with a mean age of 58 ± 13.1 years (median 58; range 18–91), a mean symptom duration of 11 ± 9.9 years (median 7; range 1–64), and a mean time since RA diagnosis of 10 ± 9.2 years (median 6; range 1–59). Half the patients (54%) had sought advice at hospitals and 31 had a history of surgery for their RA (joint replacement, arthrodesis, and/or synovectomy).

Assessment of RA activity. We computed the DAS28 score in 821 (98%) patients. Mean tender joint count was 6.6 ± 6.0 (median 5; range 0–28), and mean swollen joint count was 3.9 ± 4.0 (median 2; range 0–26). Mean ESR was 25 ± 17.6 mm/h (median 20; range 1–106). Mean disease activity as assessed by the patients on a 0–100 VAS was 43 ± 24.3 (median 43; range 0–100). Based on these values, 31% of patients were in remission, 21% had mildly active RA, 41% had moderately active RA, and 7% had very active RA; thus, in all, 48% of patients had active disease. Disease activity as assessed by rheumatologists on a 0–100 VAS was 38 ± 22.6 (median 33; range 0–97). Mean plasma CRP concentration was 14.5 ± 15.5 mg/l (median 8.8; range 1–111).

Table 2 reports details on patients according to disease activity as assessed by the DAS28 score. Mean age and female-to-male ratio were higher in the group with very active RA. Worse DAS28 scores were associated with greater disease activity, as assessed by rheumatologists, and with higher CRP levels. The proportions of patients with radiographic structural lesions or a past or current history of rheumatoid nodules increased with the DAS28 score, whereas no differences were found for other extraarticular manifestations of RA.

Previous and current treatment of RA. Three-quarters of the survey patients (75%) had been treated with at least one DMARD (median 1; range 0–6). A history of 3 or more

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Table 1. Characteristics of the 492 rheumatologists who participated in the PRISME survey.

Characteristics	PRISME, n = 492, n (%)	National Reference, %
Sex		
Male	306 (62.2)[aa]	70.8
Female	186 (37.8)[aa]	29.2
Age, yrs		
< 45	178 (36.2)	36.2
45 to 49	122 (24.8)	23.8
> 50	188 (38.2)	40.0
Mean ± SD, median (range)	47 ± 7, 46 (26–68)	—
Geographic region		
Ile-de-France	88 (17.9)[a]	23.3
West	112 (22.6)[a]	17.9
Northeast	116 (23.6)[aa]	17.4
Southwest	45 (9.1)	10.7
Southeast	131 (26.6)	30.7
Community and population		
City, > 100,000	213 (43.3)	
City, 20,000 to 100,000	203 (41.3)	
Rural/semi-rural area, < 20,000	75 (15.2)	—
Type of practice		
Office practice only	249 (50.6)	53.4
Office and hospital practice	243 (49.4)	46.6

[a, aa] Significantly different from the French national reference for the same category of physicians ($p < 0.05$ and $p < 0.01$, respectively).

Table 2. Characteristics of survey patients with RA according to disease activity assessed by DAS28 score.

	Disease Activity[#]			
	Remission, N = 250	Mildly Active, N = 177	Moderately Active, N = 338	Highly Active, N = 56
Female, n (% of patients)	186 (74)	143 (81)	270 (80)	52 (93)[a"]
Age, yrs, mean ± SD	58 ± 13.2	58 ± 13.0	58 ± 13.3	61 ± 12.3[b"]
Disease activity assessed by physician on 0–100 VAS, mean ± SD	20 ± 13.6	32 ± 16.5[c]	49 ± 19.9[c']	65 ± 19.9[c"]
CRP concentration, mg/l, mean ± SD	8.2 ± 9.2	12.4 ± 14.5[d]	17.0 ± 15.9[d']	29.2 ± 19.9[d"]
Radiographic erosions, n (% of patients)	156 (62)	133 (75)[e]	261 (77)[e']	49 (88)[e"]
Rheumatoid nodules, current or past, n (% of patients)	23 (9)	33 (17)[f]	65 (19)[f']	19 (34)[f"]
Other extraarticular manifestations[§], current or past n (% of patients)	20 (8)	18 (11)	31 (9)	10 (18)[g"]

[#] Remission: DAS28 < 2.6; Mildly Active: 2.6 < DAS ≤ 3.2; Moderately Active: 3.2 < DAS ≤ 5.1; Highly Active: DAS28 > 5.1. [§] Tendinitis, pulmonary disorder, and/or Sjögren's syndrome. [a"] Statistically significant vs remission, mild activity, and moderate activity ($p < 0.05$). [b"] Statistically significant vs remission and mild activity ($p < 0.05$). [c,c',c"] Statistically significant vs remission (c), vs remission and mild activity (c'), or vs remission, mild activity, and moderate activity (c": all $p < 0.01$). [d,d',d"] Statistically significant vs remission (d: $p < 0.05$), vs remission and mild activity (d': both $p < 0.01$), or vs remission, mild activity, and moderate activity (d": all $p < 0.01$). [e,e',e"] Statistically significant vs remission (e,e',e": $p < 0.01$). [f,f',f"] Statistically significant vs remission (f,f': $p < 0.01$), or vs remission (f": $p < 0.01$), mild activity, and moderate activity (f": $p < 0.05$). [g"] Statistically significant vs remission and moderate activity ($p < 0.05$).

DMARD courses was noted in 27% of patients overall and in 46% of patients with very active RA. Most patients (90%) were currently receiving DMARD therapy, usually (85% of all patients) with a single compound; 51% of patients receiving DMARD therapy were also taking a corticosteroid. Corticosteroid therapy was used alone by 7% of patients. MTX was the most widely used DMARD, taken by 77% of patients; 11% of patients were taking another immunosuppressant, 4% an antimalarial and 4% sulfasalazine. Current DMARD use according to DAS28 scores is reported in Table 3. The proportion of patients taking MTX was significantly greater in groups in remission or with mild activity, versus

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Table 3. Disease-modifying antirheumatic drugs (DMARD) and corticosteroids used at the time of the survey visit, according to disease activity assessed by DAS28 score. Values are number of patients (%).

	Disease Activity[#]			
	Remission, N = 250	Mildly Active, N = 177	Moderately Active, N = 338	Highly Active, N = 56
At least one DMARD	238 (95)[a]	158 (89)	292 (86)	51 (91)
Methotrexate	210 (84)[b]	143 (81)[b']	241 (71)	36 (64)
Immunosuppressant	19 (8)	12 (7)	44 (13)[c]	12 (20)[c"]
Gold salts	2 (1)	— (0)	3 (1)	— (2)
D-penicillamine	— (0)	— (0)	2 (1)	— (0)
Antimalarial	10 (4)	5 (3)	16 (5)	1 (2)
Sulfasalazine	10 (4)	7 (4)	7 (2)	6 (11)[d"]
Corticosteroids	125 (50)	97 (55)	214 (63)[e']	36 (64)
NSAID, analgesics	8 (5)	9 (5)	14 (4)	3 (6)

[#] Same definitions as in Table 2. [a] Statistically significant vs mild and moderate activity ($p < 0.01$). [b,b'] Statistically significant vs moderate (b: $p < 0.01$) or vs high activity (b': $p < 0.05$). [c,c"] Statistically significant vs remission and mild activity (c: $p < 0.05$; c": $p < 0.01$). [d"] Statistically significant vs remission and mild activity ($p < 0.05$) and moderate activity ($p < 0.01$). [e'] Statistically significant vs remission ($p < 0.01$).

groups with moderately or very active disease. Conversely, the proportion of patients who used other immunosuppressants or sulfasalazine was higher in the group with very active RA. Concomitant corticosteroid therapy was more common among patients with moderately active or very active RA (Table 3).

Mean duration of MTX use was 3.1 ± 3.1 years and mean current dosage was 11.1 ± 3.4 mg per week. However, 16% of patients were on a dosage of 15 mg/week and an additional 4% a dosage greater than 15 mg/week. Mean duration for corticosteroid use was 4.8 ± 5.3 years and mean dosage was 7.7 ± 3.7 mg/day; a current dosage greater than 10 mg/day was noted in 5% of patients overall and in 9% of those with active RA.

Changes in RA treatment during the office visit. Treatment was changed in 168 (20%) patients overall. The proportions of patients whose treatment was changed were significantly higher in the groups with moderately active (25%; $p < 0.01$) or very active (27%; $p < 0.05$) disease versus those with remission or mildly active disease. The treatment was left unchanged in 78% of patients overall, and in 72% and 70% of patients with moderately active and very active RA, respectively (Figure 1).

The most common treatment changes consisted in initiation of a DMARD (80% of changes) and/or a corticosteroid (56%) or an analgesic/nonsteroidal antiinflammatory drug (12%). Among patients started on a new DMARD, 66% were given MTX, 8% another immunosuppressant, and 8% an antimalarial. In 74% of patients whose treatment was changed, a single drug was prescribed; of the patients prescribed a new single-drug treatment, 60% were given MTX.

Of the 168 patients whose treatment was changed, 110 patients were taking MTX after the visit. Among these 110 patients, 47% had their dosage increased (from a mean of 7.5 mg/week to 12.7 mg/week), 8% had their dosage decreased (from a mean of 13.2 mg/week to 9.6 mg/week), and 4% were put on MTX therapy (in a mean dosage of 9.2 mg/week). After these changes, the mean MTX dosage in the 110 patients was 11.8 ± 3.3 mg/week. Of the 110 patients, 20% were prescribed a MTX dosage ≥ 15 mg/week.

In the group in whom treatment was changed, 94 were on corticosteroids after the visit. Of these 94 patients, 22% had their dosage increased (from a mean of 8.0 mg/day to 18.1 mg/day), 36% had their dosage decreased (from a mean of 8.5 mg/day to 5.9 mg/day), and 12% began corticosteroid therapy (mean dosage 11.2 mg/day). Following these changes, the mean corticosteroid dosage was 10 ± 13.0 mg/day; 11% of patients were on a dosage greater than 10 mg/day.

Patient eligibility for biological therapy. Figure 2 reports the results of our assessment of patient eligibility for biological therapy according to liberal and conservative criteria. With the liberal criteria, 194 (23%) of all survey patients were eligible for biological therapy, as compared to 93 (11%) patients with the conservative criteria. Our survey rheumatologists considered initiating an anti-TNF-α agent for 16% of patients overall; 37% and 39% of patients eligible according to liberal and conservative criteria, respectively; and 23% and 48% of patients with moderately active and very active RA, respectively. The reasons given for considering biological therapy were ineffectiveness of the current treatment (10% of all patients), progressive/destructive disease (5% of all patients), adverse effects of the current treatment (3% of all patients), and patient-related factors (mainly advanced age, 2% of all patients). The main reasons given for not considering biological therapy were assessment of the disease as stabilized (54% of patients overall, 46% of those with moderately active disease, and 16% of those with very active disease, as assessed by the DAS28) or as nonprogressive or mild (13% of patients overall, 11% of those with moderately active disease, and 5% of those with highly active disease), lack of longterm data on biological agents (6% of patients overall), improvement in the

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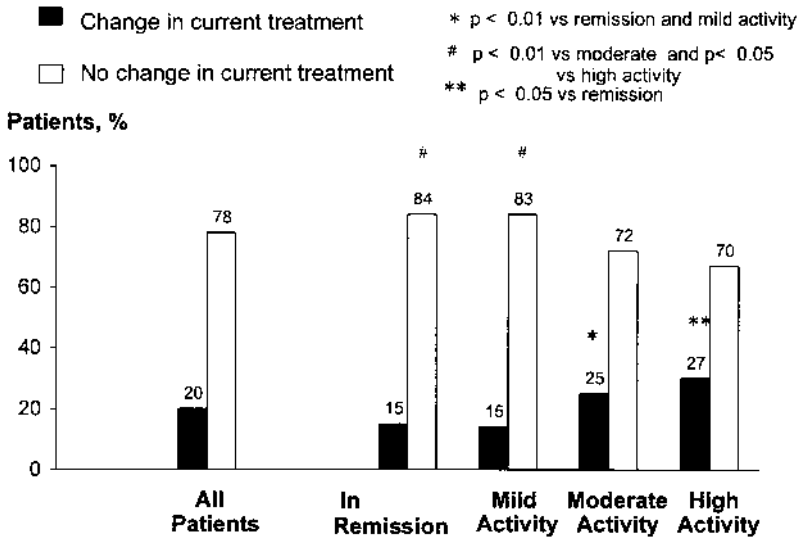

Figure 1. Treatment changes made by rheumatologists during the survey visit based on disease activity as assessed by the DAS28 score.

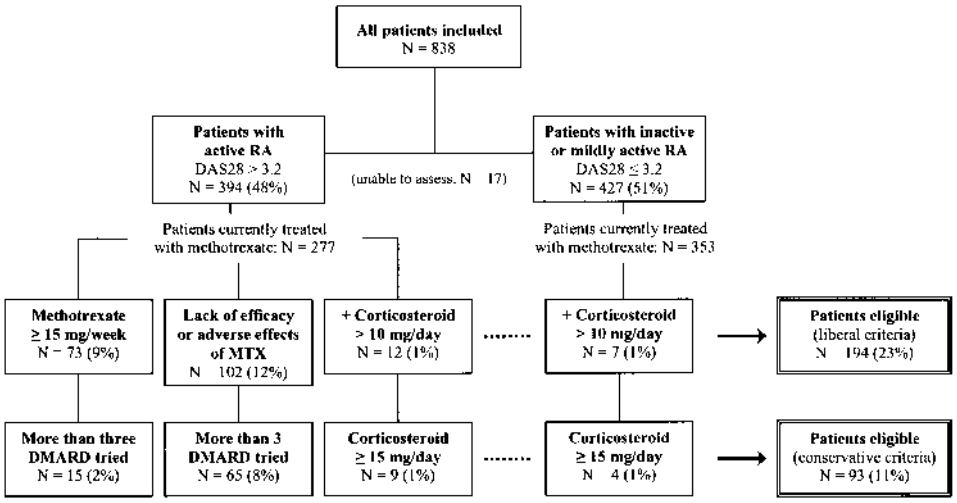

Figure 2. Eligibility of RA patients for biological therapy based on liberal and conservative criteria as defined for our study.

patient's condition (5% of patients overall), recent onset of the disease (5% of patients overall), risk of infection (1% of patients overall), and miscellaneous reasons.

DISCUSSION

Because RA runs a fluctuating course, its management requires repeated reappraisal of disease activity and treatment effectiveness. Factors that hinder accurate monitoring of RA activity include the unpredictable course of the disease and the interindividual variability in clinical expression[15]. Standard comprehensive indices consisting of more than one variable have been developed to assist in monitoring disease activity. Both the ACR index[16] and the European League Against Rheumatism (EULAR) DAS index[17] have discriminant validity and correlate with disability and radiological progression. The DAS28 is a simplified version of the DAS in which only 28 joints are evaluated. The DAS28 has been validated and is widely used to assess RA activity. Abacuses and dedicated pocket calculators are available for DAS28 computation. The DAS28 was used in the PRISME survey to assess RA activity.

The low mean number of patients with RA seen by a rheumatologist by week (5.1 ± 3.1) may be explained by the wide scope of the field of rheumatology in France, which includes all joint and periarticular diseases, as well as low back pain and bone diseases. The characteristics of the survey patients were comparable to those in 2 earlier RA surveys in France[18,19] regarding the strong female predominance (~80%), mean age (57–58 yrs), symptom duration (10–11 yrs), presence of rheumatoid nodules (15–20%), and radiographic joint lesions (70–80%). PRISME is the first survey in

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France that assessed RA activity using the DAS28 score. DAS28 scores were also determined in 2 recent European surveys in populations comparable to ours for sex ratio and disease duration[20,21]. One was conducted in Spain and found a mean DAS28 score of 3.4 ± 1.2. In the other survey, the mean DAS28 score was 5.3 ± 1.0 in Lithuania and 4.4 ± 1.4 in Norway, supporting the possibility that RA may be more severe in northern European than in Mediterranean populations[22].

The remission rate of 31% using DAS28 seems quite high, and could reflect that DAS28 may not be an appropriate measure of remission, as suggested by Makinen, *et al*[23-25]. In our study, we focused on the DAS28, and all available data necessary to calculate percentage of patients according to other remission criteria were not available. In a future study, it would be interesting to compare them in routine practice.

One of the objectives of the PRISME survey was to determine the proportion of RA patients with persistent disease activity despite MTX therapy. MTX is currently recognized as the standard DMARD, due to its excellent efficacy and usually good tolerability even with longterm use[26]. ACR guidelines define unacceptable RA activity as continuing disease activity after 3 months of maximum therapy. In our survey, all patients had received at least one course of MTX treatment, and 77% had been on MTX for more than 3 years on average. However, active RA, defined as a DAS28 score > 3.2, was noted in 48% of patients. Although persistently active disease requires a major change in the treatment program, only 20% of patients had their treatment changed during the rheumatologist visit; the treatment was left unchanged in 78% of patients overall and in 70% of patients with very active RA. Thus, French rheumatologists seem reluctant to change treatment regimens in patients with established RA, even in the presence of marked disease activity.

No specific criteria have been defined in France for initiating biological therapy in patients with RA. In the United Kingdom, a Working Party of the British Society for Rheumatology (BSR) issued guidelines for prescribing TNF-α blockers in adults with RA. According to these guidelines, patients most likely to benefit from TNF-α blockers are those with a DAS28 score > 5.1 at 2 visits one month apart despite adequate treatment with MTX and at least one other standard DMARD ("adequate" defined as ≥ 6 months, including at least 2 months at the standard target dose, unless dose-limiting toxicity occurred; or < 6 months but ≥ 2 months at the therapeutic dose followed by discontinuation because of toxicity)[27].

In our survey, eligibility criteria for biological therapy were persistent disease activity (DAS28 > 3.2) despite current high-dose MTX therapy and/or intolerance to MTX, or an acceptable level of disease activity at the price of concomitant high-dose corticosteroid therapy. High-dose MTX therapy was defined for our study as a weekly dose ≥ 15 mg because French rheumatologists are reluctant to increase MTX doses above 15 mg/week. This is because (1) most studies of MTX in RA used 7.5 to 15 mg per week; (2) in a study of patients with active RA receiving 15 mg/week, increasing the dose to 45 mg/week failed to improve disease control[26]; and (3) French rheumatologists use low-dose folic acid in combination with MTX. Nevertheless, French rheumatologists will probably increase MTX dosage in the future as the Club of Rheumatism and Inflammation of the French Society of Rheumatology recommends the use of MTX up to 0.3 mg/kg (maximum 25 mg)[9]. An excessive corticosteroid requirement was defined as a daily dose > 10 mg prednisone-equivalent[28], as suggested by the ACR subcommittee on RA. However, because doses up to 15 mg/day were considered acceptable in several studies[28-32], we performed a second analysis with 15 mg as the cutoff.

Using our criteria, 24% of patients were eligible for biological therapy. With the additional requirement of at least 3 prior DMARD courses and at least 15 mg of corticosteroid per day, the proportion was 12%, in keeping with earlier studies reporting proportions in the 10%–13% range. However, using the far more restrictive criteria suggested by the BSR, only 5% of patients were eligible for biological therapy. These data confirm that the number of patient candidates for anti-TNF therapy may vary widely according to the criteria chosen to treat[33]. The principal difficulties for the evaluation of eligible patients are: (1) that the majority of patients seen in routine practice did not meet criteria of inclusion used in clinical trials sponsored by pharmaceutical companies to introduce biological agents[34]; and (2) the lack of a clear international recommendation.

Our survey rheumatologists considered TNF-α blocker therapy for only one-third of the patients who met the survey eligibility criteria; this proportion was about one-fourth in patients with moderately active RA and one-half in those with very active RA. The main reported reason for not considering biological therapy (62% of cases) was assessment of the disease as stabilized, not progressive, or not severe. This conflicted with the DAS28 scores, which indicated that only 52% of survey patients were in remission or had mildly active disease. Yet Fransen, *et al* showed that routine monitoring of RA activity using DAS28 led both to more changes in DMARD therapy and to lower disease activity[34]. Similarly, the TICORA study demonstrated that a strategy of intensive outpatient management of RA substantially improves disease activity, radiographic disease progression, physical function, and quality of life at no additional cost[35]. Thus, more widespread use of the quantitative DAS28 score seems likely to improve RA monitoring, thereby allowing physicians to select the best treatment in the individual patient.

Our study has several limitations. Despite financial compensation for completing the questionnaire, the rheumatologist response rate was only 29%, even after reminder telephone calls. However, this response rate is comparable to those commonly observed in comparable surveys among sim-

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ilar physician populations. The small differences between the rheumatologist sample and the reference group reflect differences and are not likely to have affected the validity of the results. The patient sample was similar to the overall group of patients seen by the rheumatologists during a predetermined week in France.

In conclusion, most patients with established RA who visit office-based rheumatologists in France receive DMARD therapy, and the most widely used DMARD is methotrexate, prescribed in three-quarters of cases. Nevertheless, half these patients have persistently active RA, defined as a DAS28 score greater than 3.2. A change in treatment was considered for only one-fifth of these patients with persistently active disease, indicating that office-based rheumatologists are reluctant to modify treatment regimens. Biological therapy is considered for only a minority of patients with active or very active RA. More widespread use in office-based rheumatology care of a validated disease activity score such as the DAS28 would be expected to improve the identification of patients with persistently active RA requiring a change in treatment. However, many factors, including risks potentially associated with DMARD modification, patient unwillingness to change their medications, or the high cost of biological therapies, may explain the low rate of treatment change in our survey. Further studies are required on the evolution of rheumatologists' prescription of biologics based on the DAS28.

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