Survey of the therapeutic management of rheumatoid arthritis in France: the OPALE study

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Abstract

Objective

To describe the therapeutic practice used in 2006 by French rheumatologists and hospital staff in RA patients, to estimate the proportion of patients currently treated with DMARDs including biologics, and to estimate the ratio of patients treated according to the SFR national recommendations.

Methods

This multicentre cross-sectional study was performed in a random sample of rheumatologists selected from a comprehensive national database and stratified by setting and region. Each rheumatologist established a registry of subsequent RA patients (first step), and filled in a detailed questionnaire for the 10 first patients from the registry (second step). At the day of inclusion, RA characteristics and DMARD treatments over the past 12 months were recorded.

Results

The majority of the RA patients were women (mean age: 58 yrs). The mean DAS 28 score was 3.6, and RA was considered as clinically and radiologically severe in almost 27.0% of the cases. In the registry part, 89.9% of RA patients were currently treated with DMARDs, and 29.3% of them received a biologic DMARD alone or in combination. In 1610 patients with detailed questionnaire records, the efficacy of the current DMARD treatment was good in almost 60% of the patients. Finally, the physician's decision was to continue the ongoing treatment in 4/5 cases.

Conclusion

In this study, RA characteristics were similar to the typical RA observed in previous studies. Biologics were major drugs in DMARD treatments with 30.1% RA patients currently treated. Modification of treatments was essentially linked to a lack of therapeutic response.

Key words

Rheumatoid arthritis, DMARDs, biotherapy, epidemiology

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Introduction

Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis. It often presents as a polyarticular inflammatory attack which provokes pain and stiffness in extremities (1), progressively destroys joints, and quality of life, ultimately reducing life expectancy (2).

During recent decades, the medical treatment of RA has been characterised by a paradigmatic change, thanks mainly to different types of biotherapy (anakinra, infliximab, etanercept and adalimumab) (3). The traditional therapeutic approach, called pyramidal and based on a progressive prescription of treatments, recommended the use of anti-inflammatory non steroidals before turning to the use of the Disease Modifying Antirheumatic Drugs (DMARDs), in cases with "erosive" disease. This approach has been replaced by a more radical approach which advocates the necessity of the DMARDs treatment in the early stages of disease (4).

Recent studies have shown the importance of combined drug treatment (combination of methotrexate and biologic DMARD), in order to control the development of RA (5). Indeed, it has been proven that such combinations are more efficient than a single biologic DMARD prescribed to patients resisting methotrexate or other medications used as single-drug treatments (6).

The initiation of treatment is particularly important. During recent decades, the development of new concepts and efficient types of therapy have emphasised the importance of treating RA at its early stage (7).

Nowadays, much evidence supports the importance of efficient DMARD treatment in the early stage of the disease, even before the first symptoms of erosion, if possible, in order to stop the process of destruction and handicap (8).

According to estimates by rheumatologists in 2000, in France 82% of patients suffering from RA are treated with a DMARD and 17% receive a biotherapy treatment (9). Some surveys were carried out in France during the last 5-6 years (PRACTIS (8), ESPOIR (10), PRISME (11)) in order to describe the treatment of RA in France. However, these studies were often limited to either in and out-patients of hospitals or out-patients of office-based rheumatologists. Considering the fact that the attention paid to the treatment of RA was growing, it became necessary to update the existing data. Changing practices were expected in line with recent recommendations.

Thus, the main objective of the OPALE study was to describe the therapeutic practice used in 2006 by French rheumatologists and hospital staff in patients suffering from mild to severe RA , and to estimate the proportion of patients currently treated with DMARDs, including biologics according to the practice of the physicians (office-based rheumatologists versus rheumatologists working in a hospital) and patients characteristics, and to estimate the ratio of patients treated according to the the French Rheumatology Society (SFR) recommendations (12).

Methods

This national observational, epidemiological, multicentre cross-sectional study was performed in 2006 in a random sample of French rheumatologists selected from a comprehensive national database (TVF database) and stratified by setting (community-based, hospital settings or both) and region (22 administrative areas).

The identification process was implemented to ensure the best representativeness of rheumatologists sample (invitation mailing sent in two waves and adjusted regarding the response rate in each strata).

The study was conducted according to the Declaration of Helsinki and in accordance with Good Epidemiological Practice (13), and applicable regulatory requirements. No ethical approval or informed patient consent was required because of the non-interventional nature of the study. As per local regulations, the study was notified to the National Council of Physicians and received approval of the "Commission Nationale Informatique et Libertés (CNIL)".

Patient selection

Patient enrollment followed a two-stage sampling design.

Registry part. Each participating rheumatologist established a registry of subsequent RA patients, up to a maximum of 20 patients by physician, consulting for RA (treated or not) during a predefined 4-week accrual period. Eligible patients were men or women aged ≥18 years with mild to severe RA according to the ACR criteria (14).

Detailed questionnaire record part. The physician had to fill in a detailed questionnaire for the maximum 10 first patients from the registry who were currently receiving a DMARD treatment or those who were prescribed their first DMARD treatment on the day of their visit. There was no exclusion criteria, except the participation in a therapeutic blinded clinical trial in RA.

Collected data

The following data were collected for each participating rheumatologist: age, gender, setting (community-based, hospital setting or both) and practice location.

The data collected for the registry included the socio-demographic characteristics of the patient (age, gender, weight), frequency of visits in the last 12 months, the history and characteristics of RA (year of diagnosis, DAS28 score and its individual components, biologic or radiological assessment, severity) and treatments (previous and current).

Other data were collected in the detailed questionnaire regarding characteristics of patients (co- morbidities), detailed RA history and characteristics (diagnosis ACR criteria, previous joint replacement, disease severity and activity, biologic assessments, physical impairment) and treatments (previous, current, and newly prescribed). Recently prescribed treatments have also been described as well as the therapeutic decision at the end of the consultation. At the time when the study was carried out, four types of biotherapy were available on the French market: adalimumab, anakinra, etanercept and infliximab.

Sample size requirement

Sample size was calculated to ensure that a sufficient patients sample is available in the sub-group of patients treated with biologic DMARDs and was based on the desired precision of the observed proportions in the descriptive analysis. A minimum sample of 400 patients was required to achieve a precision of ±3.5 to 5% for an observed proportion from 10 to 50%. Considering that 25% of them were on biologic DMARD treatment, about 1800 patients were to be included to ensure the required number of 1600 evaluable patients.

Statistical analysis

According to the objectives of the survey, the statistical analysis was mainly descriptive. Mean and standard deviations for quantitative variables and frequency by modality for the qualitative variables were calculated. When relevant, 95% confidence intervals were also presented. The primary endpoints were: proportion of patients currently treated with DMARDs, including biologic and non biologic; proportion of patients failing or having inadequate response; proportion of patients discontinuing their treatment were estimated in the overall population and in subgroups defined according to patients' characteristics or treatment patterns.

The probability for a patient to be included was higher if the patient had a higher annual rate of clinic visits, compared to a patient who came once a year. With this two-stage sampling design, patients included by rheumatologist with low activity are under-sampled and patients with frequent visits are over-sampled. This study design had therefore some biases related to the limitation of the number of patients to be included, depending on the activity of each physician and to the probability for a patient to be included, which was a function of the annual clinic visit rate. In addition, sample distribution by settings was different from the national distribution by settings (45% community-based, 26% hospital settings and 26% both). Therefore, the descriptive analyses in the overall population as for the registry and for the detailed part were adjusted to weight probability sampling to take into account sampling design based on activity of physician, type of settings and annual visit frequency.

In the detailed record part, a multivariate analysis by stepwise logistic regression was performed to identify the factors associated with a biologic DMARD treatment. Potential explanatory variables (patients', disease or physicians' characteristics) were selected by univariate analysis using the Chi-squared or Fisher's exact test for qualitative variables, the Jonckheere-Terpstra test for ordered qualitative variables, the Student *t*-test for quantitative variables. All significant variables to the threshold of 20% in the univariate analyses and with less than 15% missing data were integrated in the multivariate model. Entry and exit levels were set up at 10%. Logistic regression was performed on non-weighted data.

The patients with major protocol deviations and patients for whom weights were not calculated were excluded from the analysis.

All statistical analyses were carried out using SAS® (version 8.2; SAS institute, North Carolina, USA).

Results

Physicians who took part in the study

Among 2064 physicians who were contacted between 02/06/2006 and 22/11/2006, 570 answered and 390 accepted to take part in the study. Finally, 204 physicians from 240 medical centres added at least one patient to the study.

After exclusion of patients who did not match the selection criteria and for whom weights could not be calculated, the registry was estimated at 2783 patients selected by 196 physicians. Among them, 1610/2783 (57.8%) received DMARD-treatment.

Among the 204 physicians who took part in the study, there were 114 men (55.9%) and 83 women (40.7%) aged on average 48.1 years (±7.5), similar to the mean age of the national physicians' population (15). Among 204 physicians, 103 (50.5%) were community-based, 26 (12.7%) in hospital settings and 75 (36.8%) had both types of practice.

Patients

Among 2783 registered patients (mean age: 58.2 yrs±13.7), 77.7% were women. The average number of the visits during the past 12 months was 3.3 (SD: ± 2.2; median: 3; min-max: 0-22). Dur-

ing the past 12 months, 77.9% of the patients of the registry were rarely (rarely = visit rate lower than median) examined by the physician. In the detailed questionnaire record, among the DMARD-treated patients (n=1610), 78.1% were women. Their mean age was 58.1 yrs (±13.5). Professional activity was described for 1577 patients. Among them, 40.6% were retired, 33.5% active, 11.3% housekeepers, 1.9% on sick leave, 1.5% unemployed. Among the working patients, 73.7% were full time workers.

RA description

RA characteristics are described in Table I. The mean disease duration was 9.8 yrs ±9.7. About 39.2% of the patients had been suffering from RA for at least 10 years. In 47% of the cases, the diagnosis was made by the survey rheumatologist. According to the ACR criteria, 97.2% of the patients suffered from arthritis in the hand, 96.6% – in at least 3 joints and 94% suffered from morning joint stiffness of more than 1 hour. As for the radiological lesions diagnosed by the physician, 58.1% of the patients had at least one erosion, 54.3% had joint narrowing, and 45.7% demineralisation. Finally, 21.1% of the patients had surgery for at least one joint and 65.1% had never had surgery. The average number of the operated joints was 2.7 (± 2.3). In terms of disease severity, 19.9% of the patients had extra-articular symptoms.

The morning stiffness lasted on average 30 minutes (±49) and 45.9% of the patients had been suffering from a persistent joint flare for at least one month. Co-morbidities were observed in 34.5% of the 1610 patients from the detailed questionnaire record record. Co-morbidities were: chronic obstructive pulmonary disease and/or bronchial dilatation (4.6%), cancer history (4.6%), heart failure (3.6%), chronic or recurring infection (3.0%), renal insufficiency (2.3%), tuberculosis history (1.8%), hepatic insufficiency (1.1%). Extra-articular manifestations of RA were described: 78.2% of the patients did not have any, 6.7% had skin disorders and 4.7% had ophthalmologic disorders.

RA had a considerable impact on the professional life of 9.7% of the patients.

Table I. RA characteristics of the patients from the registry and the detailed questionnaire record for DMARD-treated patients (mean ± STD).

	Registry N= 2783	DMARD-treated patients N=1610
Age (years)	58.2 ± 13.7	58.1 ± 13.5
Mean delay from RA diagnosis (years)	9.8 ± 9.7	9.8 ± 9.7
< 2 yrs	18.5%	17.5%
[2-6 yrs[	23.5%	26.0%
[6-10 yrs[	18.0%	17.0%
≥ 10 yrs	39.2%	39.2%
Tender joints (% yes)	75.1%	75.9%
Number of tender joints (of 28)	4.8 ± 4.2	4.9 ± 4.4
Swollen joints (% yes)	59.6%	61.2%
Number of swollen joints (of 28)	3.8 ± 3.2	3.9 ± 3.3
VAS (100 mm)	32.2 ± 22.8	32.6 ± 22.9
Sedimentation rate (mm/h)	22.5 ± 17.1	22.3 ± 16.8
CRP (mg/L)	11.5 ± 15.8	11.5 ± 15.4
DAS 28 (mean±STD)	3.6 ± 1.4	3.6 ± 1.4
DAS 28 <2.6	18.8%	20.0%
DAS 28 [2.6-3.2]	12.2%	13.9%
DAS 28 [3.2-5.1]	35.2%	36.5%
DAS 28 ≥5.1	12.1%	12.5%
Missing data	21.7%	17.1%
Bone erosion on radiographs (%)	59.2%	58.1%
Rheumatoid factor +	71.9%	72.7%
Anti-CCP + (when performed)	60.5%	65.7%
Clinical severe RA	36.6%	39.6%
Radiological severe RA	38.8%	40.7%
Clinical and radiological severe RA	25.0%	27.0%

Among 1610 patients, 55.2% had no professional activity. 22.8% of the patients were functionally severely disabled by the disease in their daily life, compared to 10.3% who were not. The sick leave period related to RA for the active patients ranged from 0 to 365 days during the past 12 months (17.5±63.1 days on average).

The average number of visits during the past 12 months (detailed questionnaire record) was estimated at 3.6 (±2.2). 55.7% of the patients were regularly examined by a generalist practitioner, 14.3% by a second community-based rheumatologist, 15.2% by a second hospital rheumatologist, 10.2% by another community-based specialist and 6.4% by another hospital specialist.

RA treatment

– Description of DMARD treatment: biologic or non-biologic

Twelve months before the selection visit, 32.1% of the 1610 evaluable patients from the detailed questionnaire record had received a biologic DMARD (with one drug in 79.3% of the cases): in terms of treatments prescribed, 41.4% were etanercept, 35.7% adalimumab and 18.6% infliximab. During the past 12 months, 2.4% of the patients failed to tolerate the treatment and had to withdraw (38.4% of treatments withdrawn included etanercept, 30.1% adalimumab and 29.2% infliximab). 5.5% of the patients had to stop the treatment because of inefficacy (27.3% of treatments withdrawn included etanercept, 24.1% adalimumab and 41.4% infliximab). Non biologic DMARDs were prescribed to 99.1% of the patients. A single-drug treatment was prescribed to 50.2% of the patients, while 20.7% received 2 types of treatments. Methotrexate, representing 42.3% of DMARDs was prescribed to 86.1% of the patients. During the past 12 months, 23.4% of the patients failed to tolerate the DMARD treatment and stopped (25.6%, 22.9% of treatments withdrawn included methotrexate and leflunomide respectively). 36.5% of the patients had to stop their DMARD treatment for inefficacy (31.4%, 22.1% of treatments withdrawn included hydroxychloroquine and sulfasalazine respectively). During the 12 months prior to selection visit, the treatment was modified in 27.2% of the patients. For these patients, the mean duration of their previous treatment was 26±29 months (median 14 months).

At the selection visit, the patients were on their DMARD treatment for an average of 34±38 months (median 24 months). 30.1% of patients received a biologic treatment (in monotherapy or combined with non-biologic DMARDs) and 69.9% received only non-biologic DMARDs (in monotherapy or combined with other non-biologic DMARDs) (Fig. 1). Among 1610 patients, etanercept was prescribed to 13.6% and adalimumab to 11.7%. When a biologic DMARD was used in a combination with another drug, it was methotrexate in 89.9% of the cases. This agent was prescribed in combination to 10.2% of the 798 patients receiving non biologic DMARDs including methotrexate, with either hydroxychloroquine (34.6%) or sulfasalazine (32.7%).

– Characteristics of the DMARD treatment at the selection visit

The efficacy of the DMARD treatment at the selection visit was described according to the physician's assessment: 59.6% of the patients were good responders, 31.7% of the patients were non or partial responders (Fig. 2). For 7.8% of patients, the time from the treatment initiation was too short to see the treatment efficacy. These data were similar considering biologic or non biologic DMARDs. In 75.5% of cases, the current DMARD treatment was decided by the physician himself. The main reasons for the current DMARD prescription were: first prescription of DMARD treatment (31.8%); Partial response to previous DMARD (21.8%); non response to previous DMARD (26.2%); side effects of previous DMARD (9.0%); methods of administration of the previous DMARD (0.3%); other reason (3.0%); partial response and side effects (2.3%).

Symptomatic treatments were prescribed to 88.7% of the patients: corticoids (51.5%), non selective NSAIDs (35.9%) and analgesics (32.2%). The preferences of the patients receiving biologic treatments were described. Among 482 patients with a biologic treatment, 51.6% preferred a subcutaneous way of administration, 14.6% a bimonthly administration and 93.5% had no preferences towards a non biologic treatment.

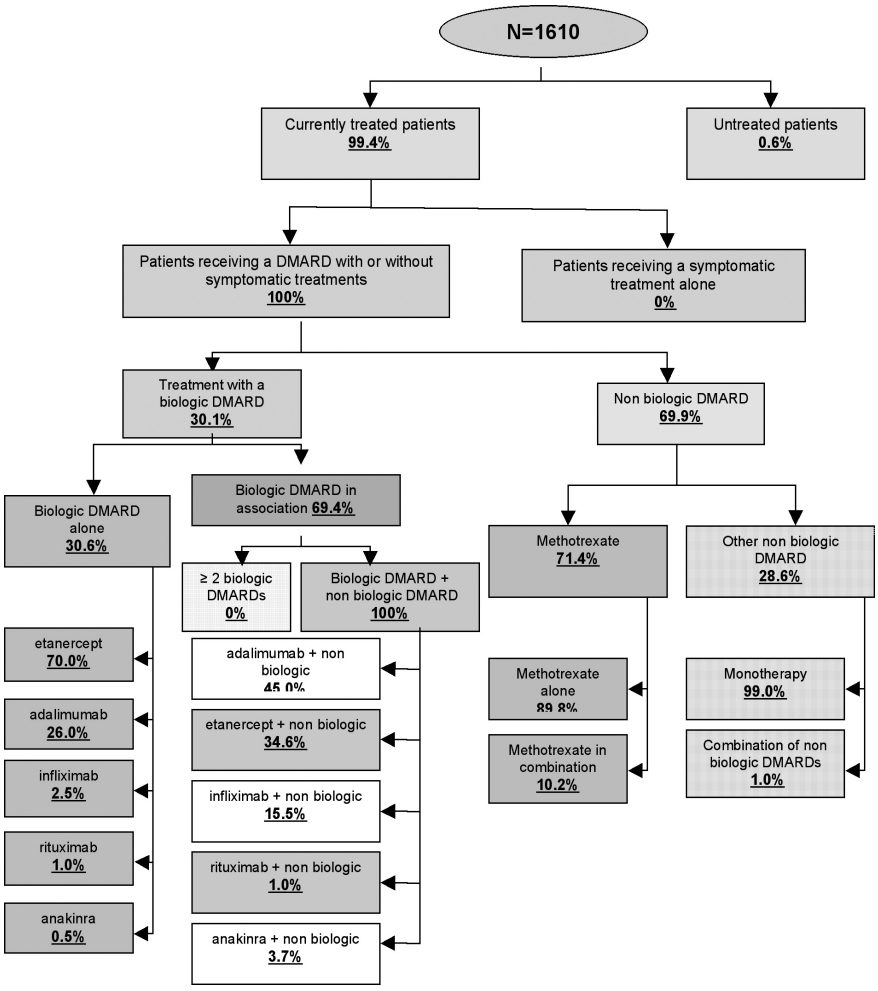

Fig. 1. description of DMARD treatment at the selection visit.

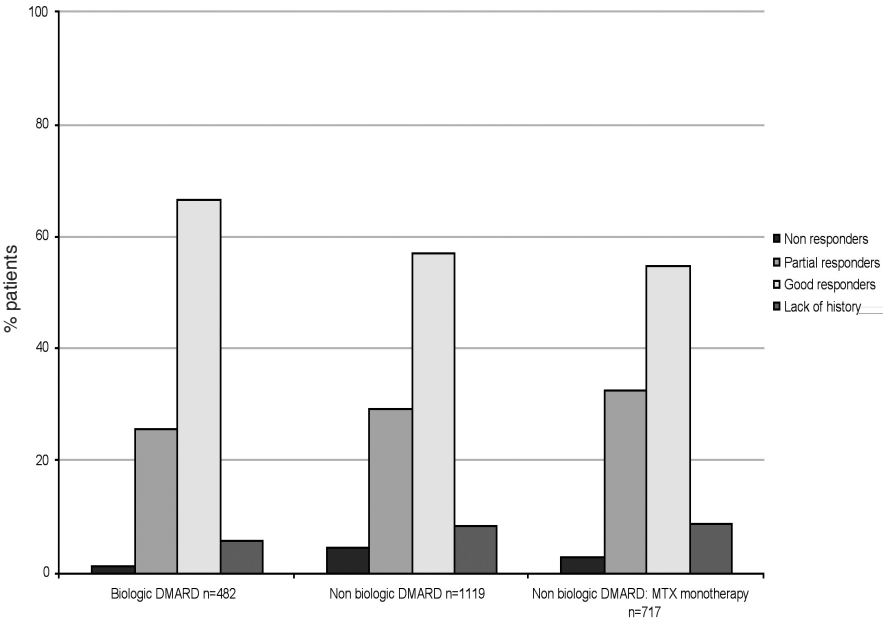

Fig. 2. Response to the current DMARD treatment at the selection visit.
0.3, 0.3, 0.5% of missing data in patients with a biologic DMARD, non biologic DMARDs and treated with MTX alone respectively.

– Description of biologic treatments

Biologic DMARD treatments were described in 482 patients. Nearly all (98.9%) of the biologic treatments were anti-TNF alpha agents. The characteristics of the patients with anti TNF are presented in Table II. In terms of biologic treatment line, 67.9% of patients were naïve, 24.1% were on first line, 4.8% on second one and 1.0% on third one and beyond. The most frequent biologic treatments prescribed on second line were infliximab (54.7%) and etanercept (26.9%). Adalimumab was the most frequent treatment prescribed on third line (92.1%).

Physician's therapeutic decision at the end of the visit

The physician's therapeutic decision at the end of the visit is shown in Figure 3. The main reasons for modification of the DMARD treatment at the end of the visit were: first prescription of DMARD treatment (8.3%); partial response to previous DMARD (47.3%); non response to previous DMARD (21.6%); side effects of previous DMARD (4.0%); methods of administration of the previous DMARD (2.9%); other reason (9.0%); partial response and side effects (0.2%).

Overall, 89.2% of patients were prescribed a treatment including DMARDs at the end of the visit. A biologic treatment was prescribed in 21.1% of patients.

Among the 108 patients on biologic DMARD only, 49.5% were receiving etanercept and 27.3% adalimubab. With regards to the 195 patients on biologic DMARD associated with another type of medicine, methotrexate alone was prescribed in 85.7% in association with adalimumab (37.3%), etanercept (28.6%) and infliximab (26.5%). Among the patients on a biologic DMARD associated with a non biologic DMARD (besides methotrexate), 41.8% were on adalimubab in combination with leflunomide and 14.7% etanercept associated with leflunomide. In 100 patients on methotrexate in combination with another non biologic DMARD, 36.0% were on sulfasalazine and 20.8% with hydroxychloroquine. Leflunomide was prescribed as a monotherapy to 43.8% of the patients who were on non biologic DMARDs (besides methotrexate). Finally, among the patients taking several types of non biologic DMARDs (besides methotrexate), 34.6% were receiving leflunomide combined with sulfasalasine and hydroxychloroquine.

The factors associated with a biologic treatment prescription were as follows: radiological (OR: 3.13 [2.04;4.76]) or clinical (OR: 2.13 [1.52;2.94]) severity of RA, age of the patients (between 40 and 50 *vs.* between 50 and 60 (reference): OR: 1.57 [1.02;2.40]), heart failure improbability (OR: 4.29 [1.41;13.05]), presence of rheumatoid factor (OR: 1.59 [1.08;2.38]), joint narrowing (OR: 1.43 [0.99;2.04], p=0.056), erosions (OR: 1.47 [0.97;2.72], p=0.070) and absence of structural progression of the disease (OR:1.37 [0.97; 1.94], p=0.074).

Table II. Description of anti-TNF treated patients.

		Infliximab alone or combined	Etanercept alone or combined	Adalimumab alone or combined
	n.	56	219	189
Cardiac failure	Yes	–	3.2%	0.9%
	No	100%	96.8%	99.1%
Presence of a contra-indication	Yes	6.4%	19.3%	9.0%
	No	89.1%	79.6%	75.2%
	Missing data	4.4.%	1.1%	15.9%
Contra-indications	Infliximab	–	2.2%	1.4%
	Etanercept	–	–	1.8%
	Methotrexate	–	5.5%	1.9%
	Leflunomide	3.5%	2.7%	2.9%
	Sulfasalazine	2.9%	5.1%	0.9%
	Hydroxychloroquine	–	0.3%	0.9%
	Gold salts	–	7.4%	1.9%
	Cyclosporine	–	–	0.8%
	D-Penicillamin	–	0.5%	1.2%
	Azathioprine	–	2.5%	–
Duration of treatment at the selection visit (months)	Mean ± STD	43.4 ± 24.1	23.8 ± 29.5	26.9 ± 26.9
	Median	54.4	23.4	26.4
	Quartile Inf; Sup	19.4; 59.4	10.4; 31.4	10.4; 38.4
	Min; Max	2.4; 73.4	0.4; 319.4	0.4; 192.4

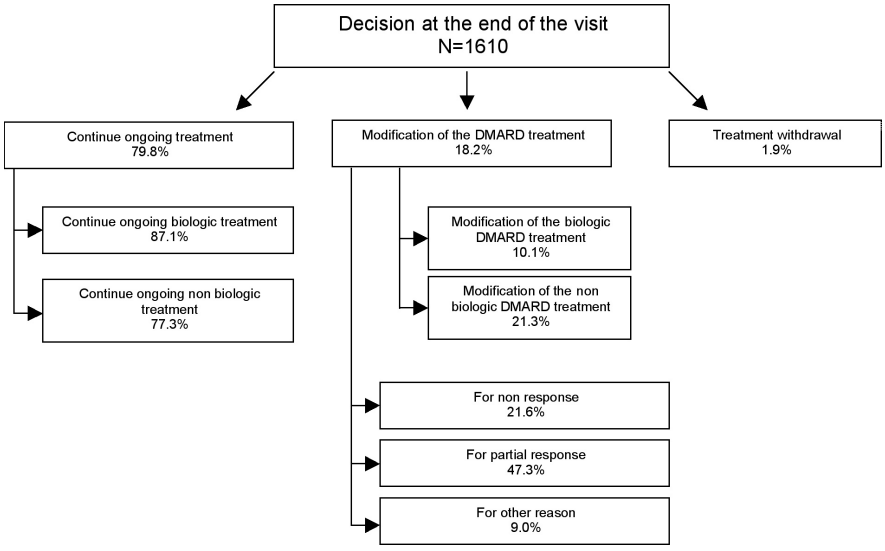

Fig. 3. decision of the physicians at the end of the selection visit.

Discussion

The objective of this epidemiologic study was to thoroughly describe the

current methods/modalities used by rheumatologists in France to treat patients affected by rheumatoid arthritis. The study design required rheumatologists to survey approximately 20 RA patients in a registry and to provide treatment details in the first 10 of them receiving DMARDs.

The characteristics of RA patients managed by French rheumatologists were described and we found that the description of the RA population was consistent with previous studies. The treatments were also thoroughly described in our study. In the Registry part, we found that 89.9% of RA patients were currently treated with DMARDs, and that 29.3% of them received a biologic DMARD alone or in combination. In 1610 patients from the detailed questionnaire part, the efficacy of the current DMARD treatment was good in almost 60% of the patients. Finally, the physician's decision at the end of the routine visit was to continue the ongoing treatment in 4/5 cases.

Our objective was also to catch, as much as possible, the representativity of the current RA population in our sample. Therefore, a special effort was made with the statistical methods. In order to improve the representativity of the selected population sample, the adjusted data have been analysed. The characteristics which have been taken into consideration referred to the activity of the physicians, the type of their activity and the number of annual visits of their patients.

Taking into consideration the disparity of the physicians participating in this study, it is important to pay attention to the activity of every medical centre: a centre identifying 20 patients within 15 days would not have the same level of activity as a centre identifying 10 patients per month. Thus, the patients recruited by the physicians with a more important activity had a higher impact than the rest of the patients. The weighting procedure allowed for controlling for imbalance in representation according to physician activity.

In our study, RA characteristics appeared to be quite similar to other recent European studies. In Spain, a prospective study has evaluated the incidence of RA. Among 362 patients with RA diagnosed according to the ACR criteria, 69.3% were women, 51.7% were RF positive, mean age was 54 years and 70% had polyarticular disease (16). In the QUEST-RA study which analysed RA populations of 25 different countries all over the world, the typical RA cohort was represented by middle-aged women, generally greater than 70% in any RA cohort, with a mean DAS28 score of 4.3 in females and 3.8 in males. This study was established in 2005 to promote quantitative assessment in usual clinical care. The French group of 389 patients had a mean DAS28 score of 3.7 and mean disease duration of 12.8 years. However, some differences in disease activity, severity and treatments were observed between our study and the QUEST-RA study overall. In fact, RA treatment distribution was very different across the 25 countries and unlike our study, a full description of the RA treatment was not a main objective for the authors (17). Indeed, in this study rheumatologists surveyed RA patients irrespective of the degree of severity of the disease, which may explain why the rate of combination DMARD therapy was as low as 10%. This finding should be matched with the average DAS28 of 3.6.

Concerning classical non biologic DMARDs, methotrexate was confirmed as the anchor drug in our population prescribing in 71.4% of patients with only non biologic current treatments, more than 2/3 of non biologic DMARDs. In a previous observational study in France in the year 2000, DMARDs were prescribed to 82.1% of the patients and methotrexate was prescribed to 500/911 patients (18). In the QUEST-RA study, 62.5% of the total patients were taking methotrexate (17). In the present study, DMARD prescription concerned 89.9% of the RA patients which is a little higher compared to previous studies in France (18). It is probable that national guidelines and the recognition of the treatment window of opportunity in patients with RA necessitating early therapy have changed the therapeutic methods of rheumatologists. In Sweden, DMARD prescriptions, particularly for methotrexate, increased from 1997 to 2001 independently of patients characteristics (19). These authors showed that patients in district hospitals were less likely to be prescribed DMARDs than those in university hospitals independently of confounding factors. In our study there was no statistical difference between hospital-based and community-based rheumatologists.

The mean time from RA diagnosis was approximately 10 years. However, the study did not collect information as to both the degree of severity at diagnosis and the evolution of the disease severity throughout the disease duration. It was not determined whether patients received early aggressive treatment following the RA diagnosis. In France, the ESPOIR cohort study collects data on patients presenting with early RA and factors determining a DMARD initiation in early RA are studied (20).

Major achievements have been reached in the treatment of RA during the past decades mainly due to the development of biologics (21). The prescription of biologics in our study, which concerned 30.1% of the RA patients receiving a DMARD, is obviously in progression compared to the year 2000 when the first biologics were marketed in France. With the licensing of anti-TNF alpha inhibitors, the national French rheumatology society (SFR) set up recommendations in order to guide the prescription of this new generation of drugs (22). Our study reflects the prescription of rheumatologists in real life, but was not designed to analyse their strategy in parallel with disease activity. However, according to a recent study, Fautrel *et al*. showed that in France, there was a remarkable convergence between rheumatologist's opinion and national SFR guidelines (23). Another study in the Swedish RA register analysed the proportion of RA patients prescribed DMARDs between 1997 and 2001, and showed that the formulation and promulgation of national guidelines may have influenced the prescription of DMARDs. Utilisation of biologics increased in France between 2000 and 2006 and this trend was also observed in the US RA popu-

lation where an increase from 3% in 1999 to 26% in 2006 was reported in two cohorts of RA patients (24). Current care guidelines, which require sufficient disease control when deciding on continuing biologic therapy, could also help to evaluate the cost-effectiveness of biologic therapy in real life clinical settings (25).

Physicians' therapeutic decision at the end of the visit was to renew the current treatment in almost 8/10 cases in our study. One can consider that rheumatologists were conservative in their choice of treatment. A previous survey in France showed that a change of treatment was rarely considered by office-based rheumatologists even if methotrexate treated patients with RA had active or very active disease (26). In our study, we could not compare directly disease activity to the choice of treatment. We showed that in case of a modification of treatment, the major reason was a lack of response to the current DMARD treatment in around 7/10 cases. At the time of the study, biologics were mainly anti-TNF alpha treatments, and we can hypothesise that the arrival of new biologics would change the trends in DMARD prescription in France.

Finally, through this first large epidemiological study of RA patients managed by rheumatologists in France, we found that RA characteristics were similar to the typical world RA population and that almost the total RA patients were currently treated with DMARDs, accounting for the achievements reached during the past decades in the treatment strategies. In half a decade in France, biologics have been recognised as major drugs in DMARD treatments with 30.1% RA patients currently treated. Modification of treatments was essentially linked to a lack of therapeutic response. New biologic therapies on the market since 2006 and on development will have the ability to continuously improve RA control, and should be monitored.

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