A Survey of Barriers to Treatment Access in Rheumatoid Arthritis

Country Annex Report: France

October 2009

1 Interviews

In France, five physicians and two representatives of patient organisations were interviewed. These interviewees came from Besançon, Montpellier, Nice and Paris. The physicians comprised two hospital-based and two office-based specialists, and one GP.

2 Environment

France's healthcare system is one of the most generous (and least controlled) in Europe. The system is fee for service, and consumption is essentially unlimited. The state insurance extends to 99% of the population, with coverage levels of 35% for non-essential care, 65% for drugs, consultations and tests, and 100% for hospitalisation and all costs for patients with chronic illnesses.

However, 90% of the population has complementary insurance, which covers any remaining costs or excess charges above the official tariff in the private sector. In 2006, 39.4% of all specialists were authorised to bill above the official insurance tariff and total excess billings were 15%. For all physicians, these figures 24.9% and 10.9%, respectively [1]. In rheumatology, 44% of specialists were authorised to bill above the insurance tariff, and in 2006 such billings were estimated at 16.5%: €45 million out of a total of €263 million.

RA has been recognised as a serious chronic illness for a long time, and currently around 60–70% of all RA patients are classified as ALD (affectation de longue durée), and are therefore reimbursed 100% for RA-related healthcare costs.

In France there is an estimated prevalence of RA of 310–500 per 100,000 head of population [2]. One small study found a lower prevalence in the north compared with the south [3], despite a slightly higher incidence in the north vs. the south. The study is too small to draw any conclusions, but the findings may indicate a demographic bias, since it is not unusual for pensioners in France to move south. According to the Innovative Medicines Initiative, there are an estimated 238,000 RA patients in France [4].

There are two national treatment registries, RATIO [5] and AIR-PR, and a prospective follow-up cohort of patients with early RA, ESPOIR.

- The RATIO registry collects nationwide data on opportunistic infections, severe bacterial infections and lymphomas in 100 patients with a past or present history of anti-TNF treatment in France. It is a three-way partnership between learned societies, pharmaceutical companies and institutions (the French research institute INSERM and the French drug safety agency AFSSAPS).

- The AIR-PR (Auto-Immunité et Rituximab – Polyarthrite Rhumatoide) registry is managed by the Société Français de Rhumatologie (SFR) and the Club Rhumatisme et Inflammation and collects data on patients treated with rituximab.
- ESPOIR (Etude et Suivi des Polyarthrites Indifférenciées Récentes) was initiated in 2002/03 with the objective of enrolling patients with very early RA (<6 months) and following their treatment and disease progress. Currently, more than 800 patients are followed in this cohort, which represents collaboration between SFR, INSERM and the pharmaceutical industry.

3 Market access

Following marketing authorisation (Autorisation de Mise sur le Marche [AMM]), the Transparency Commission (Commission de la Transparence) – whose membership includes representatives of the national healthcare insurance body ('Sécurité Sociale') – scores each new drug on its medical benefit ('Service Medical Rendu' [SMR]) and on the improvement in medical services associated with it ('Amélioration du Service Médical Rendu' [ASMR]). Reimbursement is then determined by another body, the Comité Economique, based in part upon the ASMR grading. Normally, drugs used in hospitals are either fully reimbursed (by the national health insurance) or not covered at all.

Pharmaceutical prices have been controlled for a long time, and consequently are among the lowest in Europe. However, since the mid-1990s, when pharmaceutical companies started to launch new drugs at the same or similar prices across Europe to avoid parallel trade, new drugs are basically priced at the European average price. In particular, a decision was made in the early 2000s to fund novel biologics that provided a significant additional medical benefit at the 'asking' price. However, there is often an associated obligation to perform post-launch observational studies. The consequence of this, in combination with free access to GPs and specialists, has led to France being one of the countries with best access to biologics, not only in RA but also in other areas such as oncology and multiple sclerosis. Traditional volume controls still apply to biologics, i.e. companies must still negotiate price volume contracts with the government – but in the case of biologics the government is particularly generous.

4 Guidelines

The first national guidelines for RA care were published by the national health insurance company in 2002 (CNAM), and as a result were indirectly linked to reimbursement. In 2005, the scientific society SFR elaborated on the guidelines, primarily to provide guidance on the use of biologics [6]. In 2007, a new guideline was published by the

government (HAS) for the overall care of RA patients, and reimbursement of costs for treatment that is outside the guidelines can theoretically be refused.

The guidelines currently appear to be the most up to date of all the national guidelines that were evaluated for this report, and are remarkably similar to the EULAR guidelines of 2007 (the authors of the French guidelines were co-authors of the EULAR guidelines). Notably, they were developed by a group of experts representing all the specialties involved in RA patient care, and representatives of both French RA patient associations (Association Nationale de Défense contre l'Arthrite Rhumatoïde [ANDAR] and Association Française des Polyarthrites [AFP]) contributed to the section on non-medical care (physiotherapy, etc.).

Due to the indirect link with reimbursement for biologics, the guidelines panel settled on a definition of severe RA that appears extremely open compared with other countries – i.e. a Health Assessment Questionnaire (HAQ) score of >0.5. The authors of the guidelines stated that, from a clinical point of view, this definition was obviously not completely in line with the European consensus, but that its purpose was to give specialists the freedom to initiate biologic treatment in patients who have a low HAQ but evidence of active erosive disease. It is currently difficult to assess the impact of these guidelines on usage of biologics as France was already one of the countries with best access between 2000 and 2007, according to an international study on access to biologics [7].

5 Provision of care

Access to specialists is direct and unlimited, although 3 years ago a voluntary system of 'GP gatekeeping' was introduced to limit specialist consultations. When choosing a GP as a 'family doctor', the visit co-payment is reduced. According to initial reports, this system formalised a pattern that basically already existed, but no data are available yet on whether specialist consultations have been reduced. However, from our interviews it appears that the system enhances the speed of referral, with patients being seen much more quickly by the specialist after a direct request (generally by telephone) from the GP compared with direct patient requests for a specialist consultation.

For GP gatekeeping to function, the number of available GPs and their qualification for gatekeeping is important, as is the number of specialists. France has a relatively high physician density, with more than 115,000 independent practice-based physicians (médecins libéraux). There are 105,000 licensed GPs, of which 61,000 were in practice in 2006, i.e. around 1 per 1,000 head of population. The total number of independent specialists was 54,000 and, of these, 8% were purely hospital based.

Special training for rheumatologists takes 4–6 years after gaining a medical degree, including a minimum of 2 years in a rheumatology hospital department.

The total number of licensed rheumatologists is estimated at 2,500. Of these 1,800 were in practice treating patients (as opposed to, for example, clinical researchers or other non-treating roles) in 2006, i.e. around 1 per 33,000 head of population, or 1 per 28,000 adults of 18 years or older. If we estimate the total RA patient population to be 230,000–250,000, this means there is an estimated one practicing rheumatologist per 140–150 RA patients. Only 3% of these independent rheumatologists are exclusively hospital based.

The consequence of these two factors – unlimited access and a good supply of physicians – is one of the highest levels of healthcare consumption in terms of volume [8]. The cost is partly controlled with relatively low consultations tariffs: €22 for a GP visit and €25 for a specialist visit.

A recent cost-of-illness study in more than 1,400 patients with RA showed annual costs per patient, at €11,700 to public payers and €21,700 to society (Table 1), were high compared with costs reported for other countries. One reason for this is the ease of service use and the wealth of care provision; another factor is the above-average proportion of patients in the sample that were treated with biologics (>20%) [8].

Despite this overall positive picture, there remain a number of issues that were in particular mentioned by the patient associations, and that are probably similar across all countries.

- Peer influence: Care is clearly best in the areas near large university hospitals (CHU, centre hospitalier universitaire) with a particular research interest in RA (Montpellier, Toulouse, Paris, Strasbourg and Lyon). Within a 30–40 km radius of the typical CHU or large hospital, which exists in all cities, access to care is better, both because the density of specialists is higher and their knowledge is better.
- Geographical distribution: In general, urban areas have better access to treatment than very rural areas, where care can be highly variable with few specialists (see below). Therefore, care in these rural areas is dependent on the individual GP's knowledge (one patients' association representative stated that good care was "like winning the jackpot").
- Education: Knowledge at the level of the GP, particularly the older generation of GPs and those in rural areas, still needs to be improved. In particular, patients with moderate or not easily diagnosed disease can still, according to a 2003 survey of the AFP, have to wait 2–10 years for a proper diagnosis [9].

Table 1. Cost of RA treatment [8]

Resource	Reference period in questionnaire, months	Users in the reference period, n (%)	Annual cost per patient in the sample (€ in 2005)	
			Public payer perspective, Mean (SD)	Societal perspective, Mean (SD)
Direct medical costs	**NA**	**NA**	**9,216 (15,483) median: 2,677**	**11,757 (17,615) median: 3,951**
Hospitalisation	**3**	**NA**	**3,856 (10,444)**	**4,356 (11,208)**
Inpatient admissions	*NA*	*223 (15.0)*	*2,922 (9710)*	*3,191 (10,201)*
Day hospitalisations	*NA*	*264 (17.8)*	*934 (3167)*	*1,165 (3937)*
Nursing home and re-education	*3*	*72 (4.8)*	*1,197 (6916)*	*1,404 (7845)*
Outpatient consultations	**3**	**NA**	**737 (764)**	**1,053 (1092)**
Physicians	*NA*	*1,364 (91.7)*	*327 (274)*	*404 (360)*
Physiotherapy	*NA*	*443 (29.8)*	*276 (488)*	*460 (814)*
Home visits	*NA*	*455 (30.6)*	*63 (142)*	*94 (213)*
Paramedical	*NA*	*467 (31.4)*	*64 (231)*	*94 (284)*
Tests (blood analysis, X-ray, MRI)	**3**	**1,309 (88.0)**	**359 (382)**	**539 (540)**
Medication	**NA**	**NA**	**3,066 (4221)**	**4,406 (6169)**
Biologics	*NA*	*397 (26.7)*	*2,487 (4230)*	*3,537 (6179)*
DMARDs	*NA*	*1,139 (76.6)*	*217 (292)*	*2,955 (453)*
Other prescription drugs	*NA*	*1,448 (97.4)*	*362 (278)*	*573 (438)*

Resource	Reference period in questionnaire, months	Users in the reference period, n (%)	Annual cost per patient in the sample (€ in 2005)	
			Public payer perspective, Mean (SD)	Societal perspective, Mean (SD)
Direct non-medical costs*	**NA**	**NA**	**136 (702) median: 0**	**4,857 (11,827) median: 110**
Devices and investments	**12**	**NA**	**70 (472)**	**504 (2057)**
Devices	*NA*	*555 (37.3)*	*51 (320)*	*120 (489)*
Investments (house or car transformations)	*NA*	*114 (7.7)*	*19 (348)*	*384 (1976)*
Services	**1**	**NA**	**66 (484)**	**965 (3085)**
Home help	*NA*	*282 (19.0)*	*0*	*863 (2965)*
Transportation	*NA*	*86 (5.8)*	*66 (484)*	*102 (745)*
Family help (informal care)	**1**	**914 (61.5)**	**0**	**3,388 (10,714)**
Indirect costs (patients <60 years of age)	**NA**	**NA**	**2,305 (5178) median: 0**	**5,076 (11,253) median: 0**
Short-term sick leave† (≤3 months)	**3**	**70 (4.7)**	**133 (802)**	**380 (2294)**
Long-term sick leave (>3 months)	**12**	**37 (2.5)**	**226 (1519)**	**643 (4317)**
Early retirement, invalidity	**NA**	**269 (18.1)**	**1,944 (5021)**	**4,060 (10,561)**
Total annual cost			**11,658 (16,834) median: 4,860**	**21,690 (26,238) median: 14,669**

*Calculations are based on the ~50% of patients who provided detailed costs: overall, 779 patients indicated having purchased a device; 299 patients indicated having made house or car transformations; 364 patients indicated using home help; 914 indicated using family help.

†Assuming that patients are reimbursed at the level of patients classified with chronic disease (ALD).

6 Diagnosis

Diagnosis is established by RA specialists only. The published data appear be outdated and unrepresentative of current practice. A study in 2003 by the SFR indicated that 50% of cases took 6 months or more from first contact to consultation with a specialist, but this study was based on treatment patterns in the 1990s. The same study also showed that 74% of GPs asked for the opinion of a specialist within 3 months and that there was a waiting time of 15 days for a consultation with a practice-based specialist and 30–45 days for a hospital-based specialist. As mentioned in the introduction, it is difficult to assess how this has changed in recent years for new patients. However, the information from interviewees indicates that the average time from first contact to seeing a specialist is currently about 6 weeks, and for patients with suspected severe disease it is less than 2 weeks.

Diagnosis is supported by a range of procedures outlined in the EULAR recommendations, i.e. physical examination, blood tests (ESR, CRP, RF, anti-CCP); however, MRI, ultrasound and X-ray are rarely used. Publicly insured patients are covered for 60% of the cost of blood tests for inflammation. There are 6.4 MRI scanners per 1,000,000 head of population, and diagnostic procedures such as MRI, Doppler and radiography are funded at the 70% level. Again, the published data appear out of step with current practice: the 2003 study referred to above found that the time from symptom onset to definite diagnosis was, on average, 2 years. However, the interviewees indicated that a new patient with active disease would currently be diagnosed within 6 months.

Conformity with two clinical practice guidelines, the Stratégies Thérapeutiques de la Polyarthrite Rhumatoïde (STPR; 2004) and the EULAR recommendations (2007), was investigated in the ESPOIR cohort study [10]. Conformity rates were 58% for STPR and 54% for EULAR, despite the fact that the ESPOIR cohort started in 2002, some years before the publication of the EULAR recommendations. Overall, 34% of patients were not receiving any DMARDs within 6 months of diagnosis, contrary to what is recommended by EULAR. The main drivers of compliance with the guidelines were patients with evidence of disease activity and the presence of indicators of a poor prognosis. The main reason for a discrepancy between the guidelines and practice was diagnostic uncertainty, i.e. difficulty in reliably diagnosing RA as early as the first consultation with the rheumatologist. The authors conclude that there was, and probably still is, a substantial gap between practice and guidelines in France. However, from the interviews it appears again that the publicity and training surrounding the start of this cohort study has improved the referral process and, particularly in urgent cases, the waiting time to see a specialist has been reduced.

7 DMARDs

Treatment is initiated by rheumatologists immediately after a confirmed diagnosis. GPs have a role in the treatment of milder cases and for renewal of prescriptions. Overall, 75–90% of patients receive a DMARD as first-line treatment. MTX (10–25 mg), leflunomide (20 mg/d) and sulphasalazine (2 g/d) are all recommended by the HAS guideline. Anti-malaria treatments like hydroxychloroquine are also used, typically in milder forms of RA. Steroids are recommended as symptomatic treatment and are prescribed to patients waiting for confirmation of diagnosis. Once DMARD treatment is initiated, steroids are tapered off and used as required. Other DMARDs licensed in France are minocycline, hydrochloroquine, cyclosporine, D-penicillamine, azathioprine and gold preparations (auranofin, myocrisin).

In up to 90% of patients the first-line treatment choice is MTX. Patients are evaluated after 6 months – every 2 months for unstable patients – for treatment response; if there is insufficient effect, then the dose may be increased or patients may be switched to leflunomide.

8 Biologics

Biologics are considered second and third-line treatments for most patients and are used in less than 5% of patients as a first-line strategy. Anti-TNFs are the first treatment option. Typically, biologics are used in patients with severe RA or those who fail to sufficiently respond to DMARDs – which is 40–60% of patients initially treated with MTX. Safety and tolerability drive the choice of biologic, with priority given to drugs with fewer side effects and longer experience. Respondents did not report issues with current infusion capacity, but constraints may be expected if more intravenously infused drugs are licensed in France. There seem to be efforts to develop infusion centres at private clinics.

- First-line biologics: Etanercept (Enbrel) and adalimumab (Humira) are the most frequently used biologics, in 80% of cases used in combination with MTX. Safety and tolerability are important criteria for this choice of drugs, which is influenced by results from the RATIO registry that reported more adverse events with infliximab (Remicade).
- Subsequent biologic use: Infliximab (Remicade) is used as a next option, but cycling of etanercept and adalimumab also occurs. Rituximab (MabThera) and abatacept (Orencia) are also used as a strategy after adalimumab and etanercept (or infliximab), with a preference for rituximab due to its less frequent administration requirements.

In 2005, Fautrel *et al.* [11] conducted a postal survey targeted at all practicing office-based rheumatologists in France to determine the eligibility of RA patients for anti-TNF therapy. In France, there is a remarkable convergence between rheumatologists' opinion and SFR guidelines regarding the main factors to consider for initiation of an anti-TNF therapy.

9 Best practice

According to HAS guidelines all patients with severe disease should be treated with MTX within 3 months of diagnosis and should be switched to biologics if there is no adequate response within 6 months. All participants in our survey estimated that around 60–65% of all RA patients in France are treated according to these guidelines, with the number approaching 100% for patients with severe active disease.

There may be several reasons for this surprisingly high compliance with guideline recommendations.

- The guidelines of 2007 did, to a large extent, simply reflect existing treatment practices. It was surprising that the GP interviewed followed almost exactly the guideline stipulations for detecting and referring patients with active disease, despite unfamiliarity with guideline contents. Similarly, the office-based specialists knew the guidelines only in overview, but seemed to treat patients exactly according to the stipulations and recommendations therein.
- That the HAS guidelines largely codified efficient existing treatment practices is also supported by the finding that, even in 2003, slightly fewer than half of RA patients were being referred within the timeframe that was later supported by the 2008 EULAR recommendations. Mean and median times from first symptom to seeing a rheumatologist were, respectively, 76 and 60 days overall; 58 and 40 days for patients scheduling directly with a rheumatologist; and 78 and 60 days for those seeing a GP first. Patients with longer access times were generally cases that were difficult to diagnose or who had mild disease.
- The fact that the official HAS guidelines are indirectly linked to reimbursement is likely to encourage adherence to their recommended practices, particularly for more expensive treatment options such as biologics.
- Adherence to guidelines is also, to an extent, the result of an earlier nationwide campaign by the SFR to educate GPs and office-based rheumatologists about the early diagnosis of patients with active and potentially erosive RA. The campaign was launched following the initiation of an 813-patient cohort study (ESPOIR) investigating the initiation of DMARD treatment in a 'real world' clinical setting.

10 Treatment consistency with recommendations and guidelines

The consistency with which the diagnosis and treatment of RA in France follows key EULAR recommendations is shown below (Table 2) both for information gathered from desk research and for that obtained from the interview panel.

In addition, Table 3 examines best practice compared to the HAS French government guidelines, as these are in some aspects more advanced or favourable than the EULAR recommendations.

All interviewees agreed that the HAS guidelines provide state of the art treatment for patients with RA, and that an estimated 60% of patients are treated according to them. Physiotherapy, pain management, etc. are not included in Table 3.

11 Conclusions

RA – like oncology and multiple sclerosis – is a disease area where novel biologic drugs are available and for which France has made the decision that these should be made accessible. Access to primary and specialist care is excellent and fast, although some regional differences persist with rural areas less well served. The national guidelines for diagnosing and treating patients with RA are very progressive and detailed, and appear to be well adhered to. Overall, one can conclude that barriers to the most advanced treatment strategies do not exist at a national level, but some limitations may exist at the regional level simply due to a lower density of physicians and more limited knowledge in rural areas.

Clearly, however, the type of healthcare provided by France is costly, as illustrated by a recent observational study [8]. Total healthcare costs (direct medical costs) amounted to €11,700. Of these, around 80% (€9,200) is covered by the national health insurance, with the remaining 20% generally picked up by the complimentary insurance organisations (Mutuelles).

If we were to extrapolate these findings to the currently estimated RA prevalence of around 230–250,000 patients, total costs to the French healthcare system can be estimated at €2.7 – 3 billion. Healthcare costs represented however only slightly over half of the total burden of RA to French society (54%), bringing the total cost of the disease to the country to €5 – 5.4 billion.

Table 2. Consistency of French RA practice with EULAR recommendations

		National practice consistent with EULAR recommendations		
	EULAR recommendation	**Desk research**	**Interviews**	**Comments**
Diagnosis	Patient presenting with arthritis is referred to and seen by a rheumatologist ideally within 6 weeks of symptomatic onset	Yes	Yes	For patients with severe symptoms
	Clinical examination for detecting arthritis includes ultrasound, power Doppler and MRI.	Varies	If needed	Once patients are referred to a specialist clinic, otherwise MRI is not used systematically
	Diagnosis requires at least the following laboratory tests: complete blood cell count, urinary analysis, transaminases, and antinuclear antibodies	Yes	Yes	
	Measurement of the following factors for patients presenting with early arthritis: number of swollen and tender joints, ESR of CRP, level of RF and anti-CCP antibodies, and radiographic erosions bodies	Yes	Yes	
Treatment	Patients developing persistent/erosive arthritis should initiate DMARDs as early as possible	Yes	Yes	As soon as diagnosis is confirmed
	Use of patient information and education programmes about coping with pain and disability and maintaining work	Yes	No	Recommendations include only formal aspects on coverage for these services. However, new program for all chronic diseases started by the government
	NSAIDs are considered in symptomatic patients	Yes	Yes	
	Among DMARDs, MTX is considered the anchor drug and should be used first in patients at risk of developing persistent disease	Yes	Yes	In moderate to severe RA

		National practice consistent with EULAR recommendations		
	EULAR recommendation	**Desk research**	**Interviews**	**Comments**
	Systematic glucocorticoids to reduce pain and swelling are considered as a (mainly temporary) adjunct to DMARD treatment	Yes	Yes	
	The main goal of DMARD treatment is to achieve remission. Regular monitoring of disease activity and adverse events guide decisions on the choice or change of DMARDs and/or biologics used	Yes	Yes	
	Non-pharmaceutical interventions, such as dynamic exercises, occupational therapy and hydrotherapy, are applied as treatment adjuncts	Yes	Yes	
Monitoring	Disease monitoring includes tender and swollen joint counts, ESR and CRP assessment at 1–3 months	Yes	Yes	For active disease
	Structural damage is assessed by X-ray every 6–12 months. Functional assessment is used to complement disease activity and structural damage	Yes	Yes	

Note: The specific wording of the recommendations has been shortened in some instances for editorial reasons

Table 3. Consistency of French RA practice with national HAS guidelines

'Negative' practice	HAS guideline (France)	'Positive' practice	Notes
	Diagnosis Suspicion of RA ♦ Morning stiffness longer than 30 min ♦ Symptoms for more than 6 weeks ♦ Arthritis in at least three joints (of the wrist and hand) ♦ Pain on pressure (hand and finger joints) ♦ Symmetric symptoms Recommendation (at first consultation, by ANY physician) ♦ X-rays of all symptomatic joints, essentially hands, wrists, feet ♦ Standard lab tests: RF, anti-CCP, ESR, CRP ♦ Additional tests: creatinine, transaminases, antinuclear antibodies, urinary analysis, thorax X-ray Confirmation of diagnosis by specialist: 1) if no doubt, start DMARD at confirmation visit 2) if in doubt, ultrasound or MRI	All interviewees use these criteria, both GPs and specialists All of these tests are ordered at the first visit with suspicion of RA. GP: tests ordered and then patient referred, generally within 6 weeks. Severe cases within less than 3 weeks. Specialist: further tests (seldom all tests available)	GP family doctor has improved the referral pattern
It can take several years to achieve a diagnosis in patients with unclear symptoms or seemingly mild disease	**Treatment initiation** Treatment initiation as early as possible – at first or second visit to specialist, within 3 months Clear information to patient at treatment start Treatment goal: ♦ Remission, low DAS, control of DAS ♦ Prevention of functional disability ♦ Limit psychosocial consequences ♦ Increase quality of life	Treatment always initiated by specialists on the second visit at latest and hence generally within 6 months	60% within 3 months, most patients within 6 months

'Negative' practice	HAS guideline (France)	'Positive' practice	Notes
	Follow-up Initial follow-up: ♦ Monthly until remission is achieved ♦ Then every 3 months ○ DAS28, global patient assessment (visual analogue scale), morning stiffness, pain, painful joints, swollen joints, CRP, ESR	Follow-up after 4–6 weeks, then every 3 months Laboratory tests as needed (depending on treatment)	
	Choice of first DMARD Mild/moderate RA ♦ MTX, starting with 10 mg (max dose 25 mg) ♦ If MTX contraindicated: ○ leflunomide (20 mg/day) ○ sulphazalazine (2 g/day) ♦ If required, local cortisone infiltrations Severe RA at start (structural lesions, systemic symptoms, HAQ>0.5) ♦ MTX plus sulphazalazine/hydroxychloroquine/cortisone ♦ Anti-TNF (+ MTX) first–line treatment ♦ If required, local cortisone infiltrations	~60–80% of patients are started on MTX directly and reassessed after 4–6 weeks First-line anti-TNF treatment is rare, max 5–10%	
	Definition of treatment failure ♦ Intolerance ♦ Lack of efficacy assessed over 12–24 weeks using EULAR criteria ○ No effect ▪ DAS >5.1 and change <1.2 ▪ DAS <5.1 and change <0.6 ○ Moderate effect ▪ DAS 3.2–5.1 and change >0.6 ▪ DAS 3.2–5.1 and change 0.6–1.2 but judged insufficient by patient and physician ♦ Continuous reduction in response ♦ Unable to stop corticosteroids	HAS guideline (and thus implicitly EULAR criteria) used by an estimated 60% of physicians	

12 Sources

In addition to the references listed in the text the following sources were used in compiling French details in this monograph.

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- Polyarthrite: DGS/ GTNDO 2003, http://www.sante.gouv.fr/htm/dossiers/losp/57polyarthrite.pdf
- Vidal recos 2008: polyarthrite rhumatoïde, http://www.vidalrecos.fr

Registries

- Observatoire RATIO = Observatoire national des infections et lymphomes survenant sous anti TNFα protocoles 1 et 2, http://www.infectiologie.com/site/ratio.php
- Registre AIR-PR: Auto immunité et Rituximab_ Polyarthrite Rhumatoïde
- Registry run by SFR, financed by Roche, contains currently around 2/3 of all patients on rituximab

Delivery of care

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Patient Associations

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Medical Treatment

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