

## THE ESPOIR COHORT

### A FRENCH COHORT OF EARLY ARTHRITIS

**Steering committee:** A Cantagrel, B Combe, M Dougados, B Fautrel, F Guillemin, X LeLoet, Ph Ravaud, A Saraux, J Sibilia.

**Coordinating centre:** Montpellier University Hospital : B Combe, JP Daures, N Rincheval

**Sponsor :** French Society of Rheumatology

#### 1. RESEARCH OBJECTIVES

**The primary objective** was to set-up a multicentre cohort of early arthritis (less than 6 months) in France that could serve as a database to studies of various natures.

**Specific objectives** are in the following domains:

- diagnosis: to help determine among clinical, biological, radiographic and immunogenetics those parameters allowing for the earliest diagnosis classification as possible, in order to target early therapy;
- prognosis: to identify early those patients at risk of severe disease by investigating among clinical, biological, genetic and sociologic factors;
- medico-economic: to identify the costs and their determinants at various disease stage;
- pathologic: to collect a databank of sera, DNA, RNA to allow for studies of transcriptoms and other genomics.

**Secondary objectives :**

- to monitor adverse events, particularly rare drug adverse events, in collaboration with other international studies
- to allow access to the data collected in this cohort study in order to facilitate new projects submitted to and approved by the scientific committee.

#### 2. DESIGN OF THE COHORT STUDY

This is a longitudinal prospective cohort study in adults aged over 18 and under 70 years from multiple regional samples recruited across France.

##### **2a. Number of subjects to include.**

A sufficient number of subject would allow to obtain reasonable estimates of practices after 10 years of follow-up and run reliable subgroup analyses. A compromise has been formulated to obtain 300 patients on a 10-year term, considered as reasonable and feasible. Data from the literature, as well as previous cohort study experiences in France have shown that proportion of loss to follow-up is in the range of 5 to 8% during the first 3 years, then stabilise between 1 and 5%, depending on many different factors. Using intermediate estimates, it would be necessary to start with 400 RA patients. Given the probability than 50% of patients will probably not turn into rheumatoid arthritis after 2 years, it was planned to include 800 early arthritis patients.

##### **2b. Inclusion criteria**

- Patients aged over 18 and under 70
- Clinical diagnosis of rheumatoid arthritis as certain or probable
- Clinical diagnosis of undifferentiated arthritis potentially becoming RA
- At least 2 inflammatory joints since 6 weeks: a swollen joint has to be observed in two articular sites and be present since at least 6 weeks
- Arthritis starting since less than 6 months
- Never prescribed DMARDs, corticoids, except if less than 2 weeks or except intra-articular injection less than 6 weeks before inclusion
- Corticosteroids could be tolerated if prescribed for 1 week or less at least 1 month before the inclusion

**2c. Non inclusion criteria**

- undifferentiated rheumatism with no potential chance to become RA
- other inflammatory rheumatisms clearly defined

**2d. Patients recruitment and follow-up**

Patients have been recruited in 14 university rheumatology department.

Each centre act as an observational centre, and do not interfere with patient management. Patients are routinely treated by private or public rheumatologists in the geographical area for recruitment will be incorporated, though not treated at the centre.

All patients have be followed every 6 months during the first 2 years, then every year by the investigator in each centre. It is currently planned to follow these patients during at least a period of 15 years but to stop after 2 years the follow-up of patients with diagnosis other than RA or undifferentiated disease.

The protocole have received a favourable approval from the Montpellier ethical committee

**2e. Databases**

Several databases have been constituted to fit in the different objectives of this project.

Clinical database is collected and computerised in each centre, then centralised in the coordinating centre (Montpellier)

Biological database follows the same route, and comprises an agreed-on list of routine investigations.

X-ray database includes at baseline a chest x-ray, both hand and wrist antero-posterior view and forefoot. At each follow-up hand, wrist and foot x-ray are collected as well as other painful joints if necessary. In some centers MRI and ultrasonography on hands have also been performed

Serum, DNA, RNA, synovium liquid and tissue will be collected and double stored in adequate and definite conditions in each of 2 biological coordinating centre (Montpellier, Paris)

**3. Current patients recruitment and follow-up**

813 patients have been recruited between december 2002 and march 2005. The 4 years database have been frozen in February 2010 and the 5 years database will be frozen in January 2011.

588 patients are still followed in the cohort.

**4. Scientific projects**

A scientific committee evaluates twice a year the different projects that are submitted to ESPOIR. Almost 60 scientific projects, (mainly clinical, translational and genetic projects) are ongoing . 14 articles have already been published and 5 manuscripts are currently under revision. ESPOIR has also served as a main or validation cohort for major international projects including CR/EULAR classification criteria for RA and ACR/EULAR remission criteria in RA

Pr Bernard Combe  
Principal Investigator and Coordinator of ESPOIR

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### ESPOIR cohort : published articles

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- 3) Devauchelle V, Josseume T, Samjee I, Dougados M, Combe B, Saraux A. Ability of oblique foot

- radiographs to detect erosions in early arthritis: Results in the ESPOIR cohort. *Arthritis Rheum.* 2008;59:1729-34.
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  - 5) Benhamou M, Rincheval N, Roy C, Foltz V, Rozenberg S, Sibilia J, Schaevebeke T, Bourgeois P, Ravaud P, Fautrel B. The Gap Between Practice and Guidelines in the Choice of First-line Disease Modifying Antirheumatic Drug in Early Rheumatoid Arthritis: Results from the ESPOIR Cohort. *J Rheumatol* 2009; 36:5; doi:10.3899/jrheum.080762
  - 6) Gottenberg JE, Miceli-Richard C, Ducot B, Goupille P, Combe B, Mariette X. Markers of B-lymphocyte activation are elevated in patients with early rheumatoid arthritis and correlated with disease activity in the ESPOIR cohort. *Arthritis. Res Ther.* 2009;11(4):R114.
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  - 8) Funck-Brentano T, Etchepare F, Joulin SJ, Gandjbakch F, Pensec VD, Cyteval C, Miquel A, Benhamou M, Banal F, Le Loet X, Cantagrel A, Bourgeois P, Fautrel B. Benefits of ultrasonography in the management of early arthritis: a cross-sectional study of baseline data from the ESPOIR cohort. *Rheumatology (Oxford).* 2009 Dec;48(12):1515-9.
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  - 10) Salliot C, Bombardier C, Saraux A, Combe B, Dougados M. Hormonal replacement therapy may reduce the risk for RA in women with early arthritis who carry HLA-DRB1 \*01 and/or \*04 alleles by protecting against the production of anti-CCP: results from the ESPOIR cohort. *Ann Rheum Dis.* 2010 Apr 13. [Epub ahead of print] PubMed PMID: 19740903.
  - 11) Cyteval C, Miquel A, Hoa D, Daures JP, Mariette X, Combe B. [Rheumatoid Arthritis of the Hand: Monitoring with a Simplified MR Imaging Scoring Method--Preliminary Assessment.](#) *Radiology.* 2010 ;256:863-9. Epub 2010 Jul 27.
  - 12) Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, Combe B, Costenbader KH, Dougados M, Emery P, Ferraccioli G, Hazes JM, Hobbs K, Huizinga TW, Kavanaugh A, Kay J, Kvien TK, Laing T, Mease P, Ménard HA, Moreland LW, Naden RL, Pincus T, Smolen JS, Stanislawski-Biernat E, Symmons D, Tak PP, Upchurch KS, Vencovsky J, Wolfe F, Hawker G. [2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative.](#) *Ann Rheum Dis.* 2010 Sep;69:1580-8 et *Arthritis Rheum.* 2010 ;62:2582-91.
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