The cohort initiative

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Population – based studies of RA

- 1950-1960
- United Kingdom, USA, Scandinavia
- What we learnt ?
  - Self limited arthritis is more common than RA
- But:
  - High prevalence of RA (2.4-6.1%)
  - Low prevalence of rheumatoid factor (19-33%)
  - RA : a benign disease

First early RA clinical cohorts

- 1960….
- Bath, Middlesex, Memphis, Lund, ERAS cohorts…

- Objectives
  - Clinical course of RA
  - Long term outcome
  - Mortality, Work disability
  - Radiological progression
  - Clinical factors of prognosis
  - Treatment pattern

- Limitations:
  - low number of patients,RA diagnosis,few data collected,old therapeutic strategies …..

First early RA clinical cohorts

- RA is a severe disease
- Poor functionnal outcome by 15 years
- Early and frequent radiological damage (70 % at 2 years)
- Poor outcome may be predicted at baseline by high number of active joints, RF positivity, socio-economic status

Recent clinical cohorts of early RA

- 1990…
- Early RA versus early arthritis
- The NOrfolk Arthritis Register, the Leiden Early Arthritis Clinic…..
- Objectives
  - Epidemiology
  - Basic and clinical research

Recent clinical cohorts of early RA

- Prevalence, incidence, risk factors for the development of RA
- Radiologic and functionnal outcome
- Mortality in RA patients
- Genetic influence
- Identification of prognostic factors
  - Baseline disease activity
  - ESR, CRP, RF, anti-CCP
  - DRB1*04 genes
  - Early erosions
  - Early effective treatment
- Development of prediction models to be used at individual level
- Treatment patterns and treatment strategies

Recent clinical cohorts of early RA

Limitations:

- They have been set up 10 to 15 years ago

- The definition and diagnosis of early arthritis have evolved

  3 to 6 months versus 2 years

- The management of early arthritis has changed

  New tools, new processes and concepts, new goals….

Early RA (...early arthritis**)**

- A major interest has been recently developed to identify, classify and treat RA patients as early as possible.

But, no gold standard for the diagnosis of RA

- no single diagnostic test for diagnosis RA
- ACR criteria are definetely inadapted in the context of early arthritis

(Very) early RA : a major issue

- Evidence that early effective treatment will clearly improve RA outcome such as joint damage and long term disability
- New very effective targeted therapies now available
- Development of new concepts in early (RA) arthritis diagnosis

    1. To identify patients with arthritis as early as possible
    2. To diagnose patients with definite arthritis other than RA
    3. To identify patients with high or low risk of persistent disease and of erosive arthritis

Early arthritis : a major issue

New goals in the management of early arthritis

- To diagnose and treat patients **very early**
- To identify patients who should require early agressive therapies
- Tight control with flexible approach
- To obtain clinical and radiological **remission**

Set up of new (very) early arthritis cohorts

Development of early arthritis clinics

Early arthritis cohorts in 2004

General objectives

- Database to improve the knowledge on RA and unclassified inflammatory arthritis (UIA)
  - Current epidemiology
  - Current clinical pattern and outcome
  - New treatments influence
  - Pathophysiologic mechanism
  - Cost to the healthcare system
  - …

Early arthritis cohorts in 2004

General objectives

- Database to improve the management of RA and UIA
  - Very early recognition
    - Early referral
    - Development of EA clinics
  - Identifications of patients with high and low risk of persistent arthritis , erosive arthritis and subsequent disability
  - Proposal of the best therapeutic strategy to each individual patient

Study & follow-up of undifferentiated early arthritis
A french multicenter cohort

Inserm
Institut national
de la santé et de la recherche médicale

L'oiseau, sigle de l'A.R.P., symbole de la liberté de mouvement, et de l'espace à conquérir.

MSD
la médecine fondée sur les preuves.

The ESPOIR Cohort

Primary objective

Multicenter french cohort of very early arthritis that could serve as a database for studies on :

- Diagnosis and prognosis
- Public health considerations :
  - Quality of life
  - Socio-economic consequences of arthritis
- Pathogenesis
- Therapeutic evaluation

Specific objectives

1- Diagnosis and prognosis

- Best combination of clinical, biologic, imaging and immunogenetic elements for diagnosis
- Early prognosis, determining « high-risk » profiles

2- Comorbidity, disability and quality of life

3- Economics

To identify direct and indirect costs and their determinants at various disease stages

4- Pathogenesis

Constitution of a bank of serum, DNA, blood and synovial cells and synovial tissue for multiple studies: genomics, micro-arrays, auto-antibodies…

One national biologic center under the umbrella of INSERM

Secondary objectives

- To observe and monitor rare events, particularly drug reactions in collaboration with other international studies
- To help to the development of early arthritis clinics in France
- To set up an educational program for rheumatologists and especially for GPs focusing on early arthritis and early referral recommendations

Inclusion criteria

- Early arthritis with possible or certain RA
- Early arthritis that may potentially develop into RA

- At least 2 swollen joints
- > 6 weeks, < 6 months
- No previous DMARD
- No steroids
- Signed consent, Social security

Exclusion criteria

- Age < 18, > 70
- Pregnancy
- Early arthritis with diagnosis other than RA

  OR with features incompatible with RA

Method

- Longitudinal prospective study: follow-up > 10 years
- 800 patients
- Inclusion period : 24 months
- Follow-up: inclusion, M6, M12, M18, M24 then once a year
- Inclusions started in December 2002.

Recruitment

- 14 regional centers with a network of private practice rheumatologists
- Several communication media have been developped to invite patients and physicians to participate
- 1 national biologic ressource center

  in charge of centralizing and managing the biologic collection
- 1 national coordinating center
  - Specific CRF and softwares
  - Management of the data collection
  - Close monitoring and quality control
- National project promoted by the French Society of Rheumatology (FSR)

Unrestricted grant by Merck (MSD), partnered by Inserm, also supported by Abbott and Amgen.

Collected data

- At each visit
  - clinical,
  - HAQ, SF 36…
  - Economic questionnaires,
  - standard biology,
  - Serum and urine samples,
  - hands and feet X Rays
- At baseline

  Blood, DNA, blood cells, synovial cells and/or synovial tissue,urine
- MRI/ ultrasonography protocols

Therapeutic trials

- Therapeutic decisions will be taken by the treating private practitioners; recruitment centers will not interfere in therapeutic choices.

- BUT therapeutic trials are possible if accepted by the rheumatologists and the patients.

Baseline characteristics n=586

	mean ± SD / %	median
•Age	47.4 ± 13.8	49.6
•Female	77.5 %	-
•Duration of symptoms (days)	138 ± 159	111
•Delay in referral (days)	103 ± 63	94
•ACR criteria	3.9 ± 1.1	4
•Patient global	60.2 ± 25.0	64
•TJC	14.1 ± 11.5	11
•SJC	7.3 ± 5.6	6
•DAS28	5.6 ± 1.2	5.6
•HAQ	0.95 ± 0.66	0.9

Baseline characteristics

	mean ± SD / %	median
ESR	29.0 ± 24.4	22
CRP	22.4 ± 31.1	10
RF	41.2 %	-
Anti-CCP Ab	29.9 %	-
Anti-nuclear Ab	34.3 %	-
DRB1*04	53.1 %	-
DRB1*01	36.8 %	-

Scientific steering committee

Steering committee :

A.CANTAGREL, Toulouse
B. COMBE , Montpellier
M.DOUGADOS, Paris-Cochin
B. FAUTREL, Paris-Pitié
F. GUILLEMIN, Nancy
X. LE LOET, Rouen
I. LOGEART, MSD Paris
A. SARAUX, Brest
J. SIBILIA, Strasbourg
P. RAVAUD, Paris-Bichat

Coordinating center :

JP DAURES, Montpellier
N. RINCHEVAL, Montpellier
B. COMBE, Montpellier

Imaging center :

A. SARAUX, Brest

Biologic center :

J. BENESSIANO, Paris-Bichat

The cohort initiative

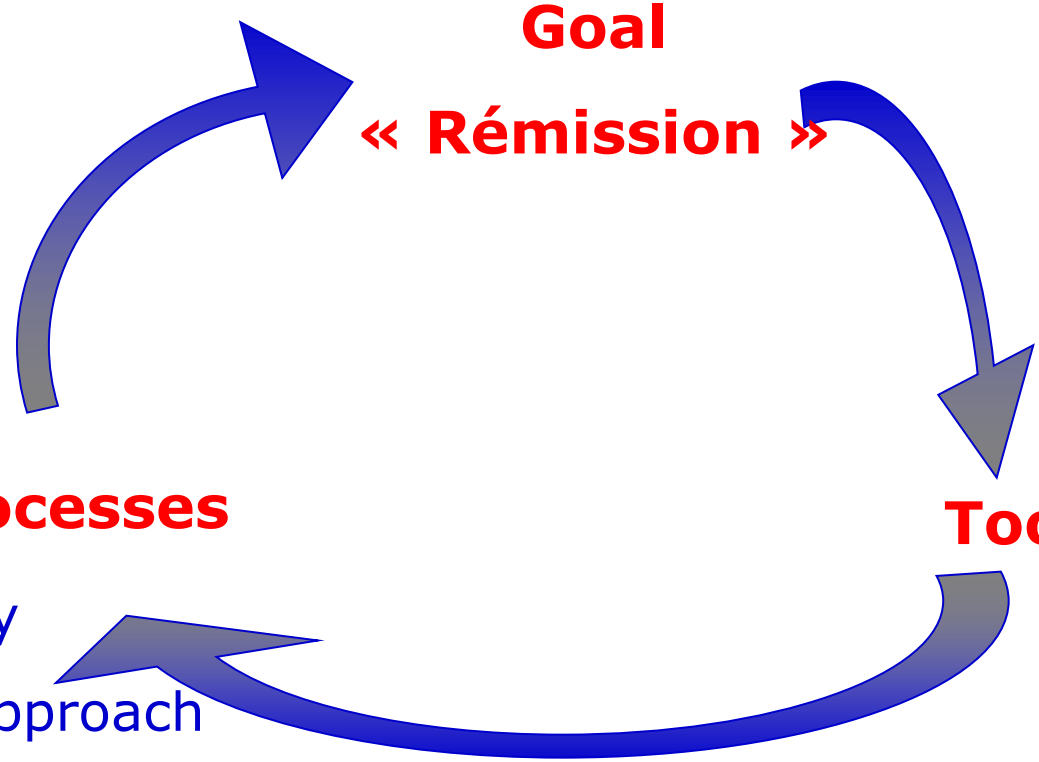
Should provide highly relevant current databases which unable us both

- To conduct clinical and basic research on RA and undifferentiated arthritis
- To improve daily clinical practice

BACK UP

RA management

- Rémission
  - Clinical
  - Radiographic
- «Low disease activity»



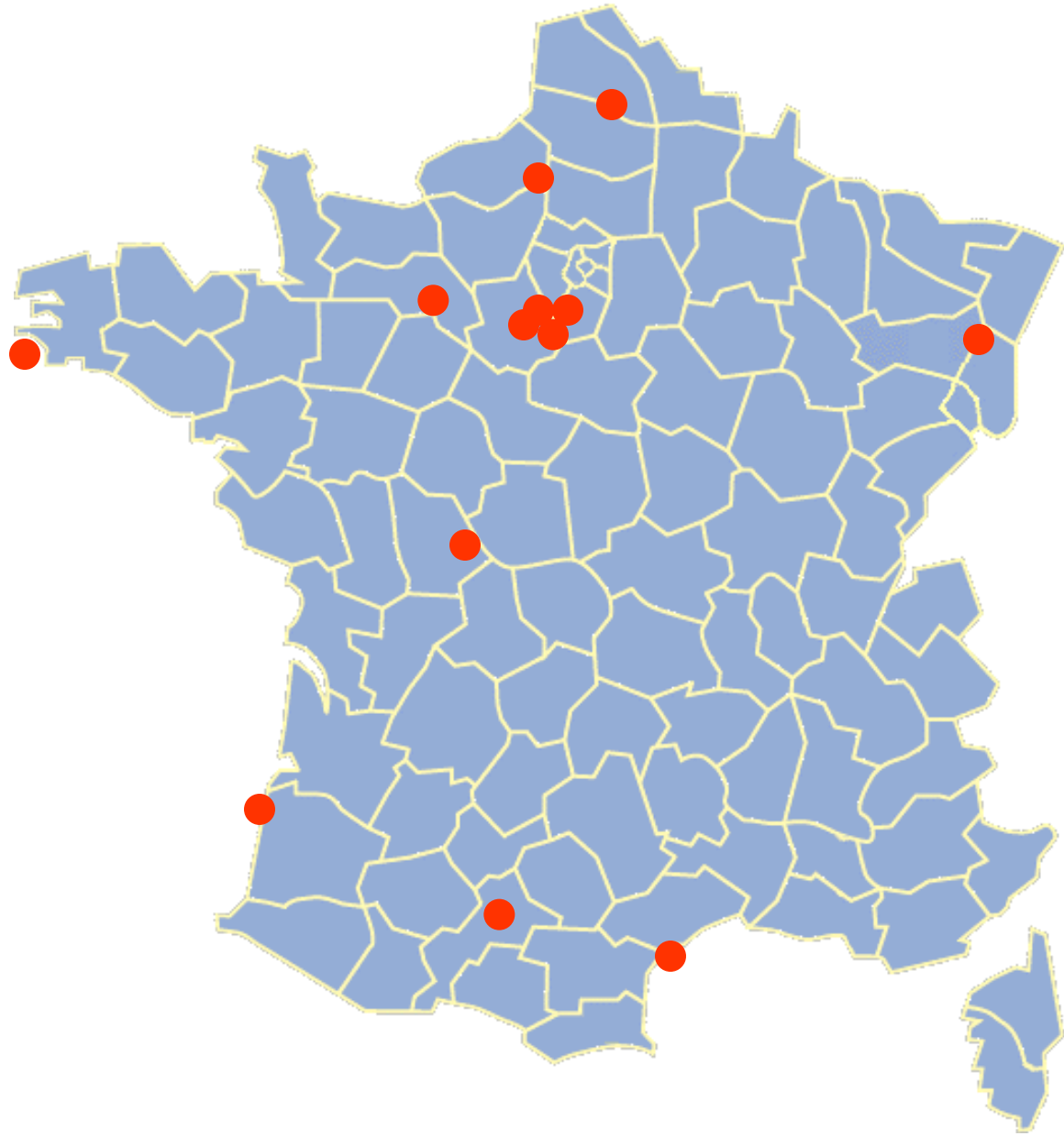
- Early treatment is key
- Aggressive therapy approach with better results
- Tight control whith a flexible approach

- More conventional DMARDs
- DMARDs combinations
- Biologics available as highly effective alternatives

Adapted from F. Breedveld, 2003

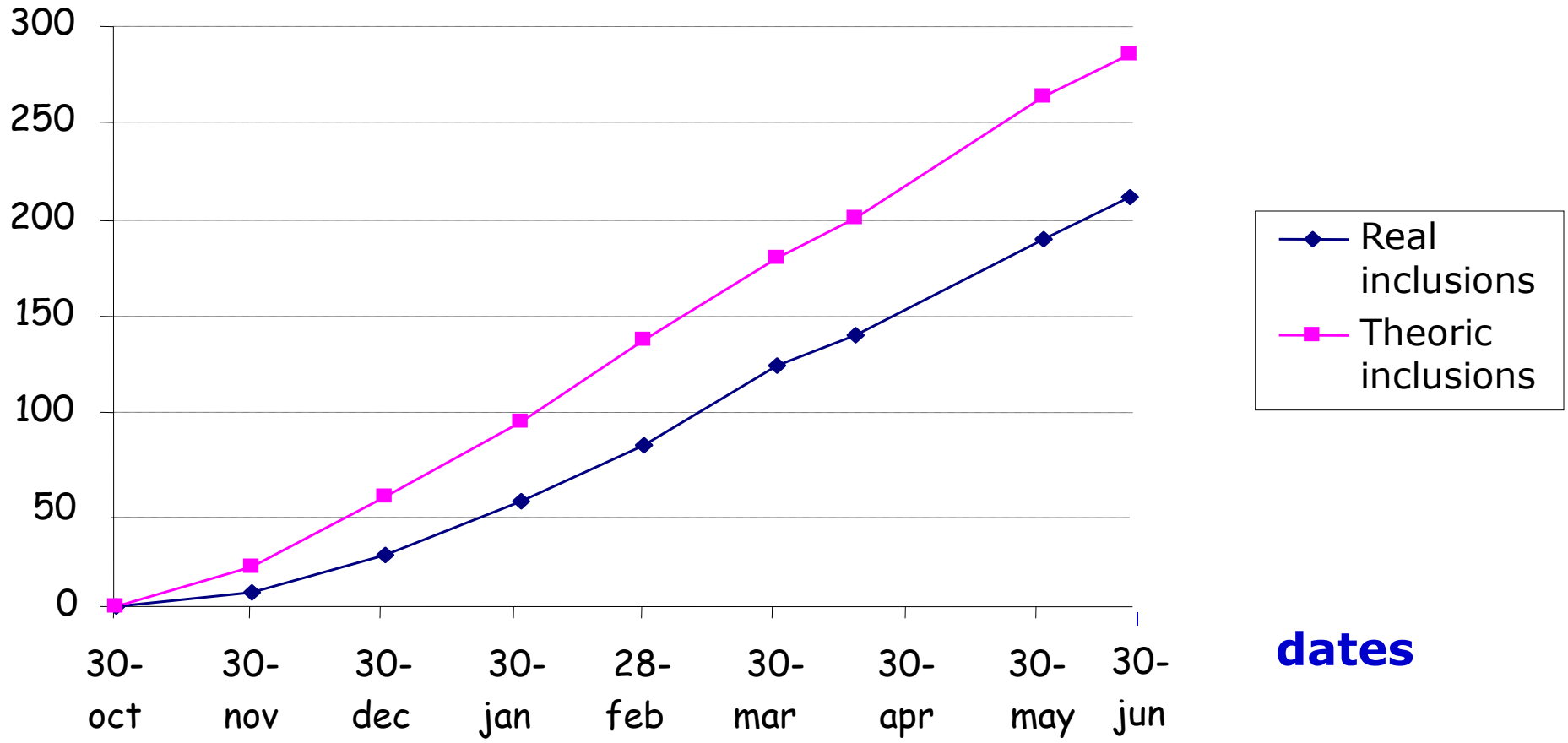
ESPOIR

Evaluation Suivi POlyarthrite Indifférenciée Récente



Inclusions

Nb of inclusion



Number of screened and included patients in each center