RaDiCo COHORT STUDY INFORMATION SHEET

RaDiCo-PID

Full title:

French National Cohort on Idiopathic Interstitial Pneumonia: From infancy to elderly

Study sponsor: **Inserm**

Principal Investigator: **Prof Annick Clement**
Service de pneumologie pédiatrique / Inserm U933
AP-HP - CHU Paris Est - Hôpital d'Enfants A. Trousseau, Paris, FRANCE

Current status of regulatory authorisations

Inserm's sponsorship agreement: 28/07/2015 / **Ethical clearance:** 06/10/2015 / **CCTIRS clearance:** 23/03/2016
CNIL authorisation: 03/11/2016 / **Information System security conformity audit (HADS):** June 2017

Study kick off date	Inclusion period	Follow-up period
15/06/2017	2 years	2 years

Background and rationale

- Idiopathic Interstitial Pneumonia (IIP)s encompass a group of diffuse infiltrative lung disorders of unknown origin that affect the lung architecture
- Characterized by a progressive and often irreversible remodelling of the alveolo-capillary barrier
- IIPs are rare diseases that can be observed at all ages, from infancy to elderly
- Patients with IIP represent a significant healthcare burden due to the chronic nature of the diseases and the lack of effective medical therapies, with associated high morbidity and premature mortality
- The nature of inciting injury and subsequent alveolar epithelium dysfunction includes genetic and epigenetic factors as well as environmental and host co-morbidity components. All together these contributors, which remain poorly understood, affect disease expression and progression
- Although IIP is most frequently diagnosed in adult patients, new information supports the view of an on-going process of lung dysfunction since early in life
- To significantly progress in IIP knowledge and care, rigorously phenotyped IIP patient cohorts combining both paediatric and adult populations are required, then covering the all disease spectrum from infancy to elderly

Study type

French multicentre, observational

Objectives

Primary objective

- Describe the phenotypic features of the paediatric and adult patients with IIP/PID, at diagnosis and during the follow-up

Secondary objectives

- Identify gene factors involved in disease initiation and progression
- Investigate the extent to which environmental and co-morbidity factors may influence disease severity and outcome
- Identify and validate biomarkers for disease diagnosis and progression

Exploratory objectives

- Production of improved strategies for patient recruitment and enrolment into clinical trials
- Development of novel strategy for patient follow-up
- Development of novel diagnostic approaches
- Evaluation of effect on natural history of disease, and tolerance of therapy, in a large population in real life
- Development of novel therapeutic approaches

Inclusion and non-inclusion criteria

Inclusion criteria

- Patient with a diagnosis of IIP/PID established on presenting history, clinical, radiological and functional and if available pathological findings, including:
  - Clinical criteria: chronic respiratory insufficiency manifestations including dyspnea/tachypnea, cough, and cyanosis during exercise or at rest
  - Radiological criteria: characteristic chest High-Resolution Computed Tomography (HRCT) abnormalities including widespread ground glass or alveolar attenuation, reticulation often associated with traction bronchiectasis, and honeycombing
  - Functional criteria: pulmonary function test abnormalities reflecting a restrictive pattern and including: loss of lung volume, vital capacity (VC), total lung capacity (TLC); reduction in the diffusion capacity of the lung for carbon monoxide (DLCO), gas exchange abnormalities, and altered ventilatory response to exercise
- Signed informed consent
- Affiliated to the "Regime National d'Assurance Maladie"

Non-inclusion criteria

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- Patients with diffuse parenchymal lung diseases caused by drug toxicity, immunodeficiency, proliferative disorders including histiocytosis, and metabolic disorders
- Patients (parents/guardians for paediatric patient) not able to approve/understand the protocol

Evaluation criteria

Evaluation criteria of the primary endpoint

- Clinical and biological characteristics of IIP/PID over time in paediatric and adults patients, based on the following assessment: Family history / Clinical parameters (respiratory and other organs) / Biological parameter / Radiological parameters / Search for infectious agents / Bronchoscopy and BAL examination / Lung function tests / Lung tissue examination (if available) / Other organ function evaluation / Treatments

Secondary evaluation criteria

- Identification of gene factors involved in disease initiation and progression
- Environmental and co-morbidity factors impact on disease severity and outcome will be performed with association studies
- Validate already published biomarkers candidates for disease diagnosis or progression

Power

- It is planned to enrol about **150 newly diagnosed IIP/PID paediatric patients** in addition to the prevalent cases (**about 400**) and a total of **2000 IIP/PID adult patients** during the 2 years recruitment period.
- Considering that all participating centres are already networking, given the incidence of the diseases, and the number of already diagnosed patients, this scheduled recruitment is realistic, and will allow achieving our primary and secondary objectives

Statistical analysis

- Descriptive multivariate analysis according to gender and mode of heritability, per visit and for the study endpoint, using the the main criteria described above and including, family history, clinical respiratory criteria and for other organs, biological and radiological covariates, infectious agents, bronchoscopy and BAL examination, lung function tests, lung tissue examination in case, other organ function evaluation and treatments, looking for relevant specific patient profiles
- Predictive analysis to explore whether some criteria might be efficient markers of disease progression/severity, according to the TRIPOD statement, and using a propensity score approach.
- Validation of already published biomarkers candidates for disease diagnosis or progression
- Search for gene factors involved in disease initiation and progression

Biocollections

- Biological resources are essential components of the IIP/PID disease diagnosis, management (i.e. biological markers of disease severity and outcome), and research. They include blood, BAL fluid and tissues (mainly lung).
- Currently, in most situations of IIP/PID, blood samples are collected and stored in standard care practice. Tissue samples are available when biopsies are indicated. In addition, some centers expand and store lung fibroblasts from tissues.
- Biobanking is performed locally at the participating centres. Each of them is responsible for its own sample collection

Number of recruiting sites	Prevalent cases retrieved / Inclusion targets vs. current status	
	Year 1	Year 2
Initiated with 20 sites in France, through the network of reference, competence and recognised expert centres for rare pulmonary diseases (adult) and for rare respiratory disease (paediatric)	**400 / 1075**	**2550**
	400 / 88	-

Public-Private Partnerships valorising the cohort resources

- Specific Research Project negotiated with BOEHRINGER INGELHEIM: Non-interventional study of the management of patients with Idiopathic Pulmonary Fibrosis (IPF) in clinical real life practice (**1,45 millions €**)
- Specific Research Project negotiated with ROCHE under discussion: Non-interventional study of the management of patients with Idiopathic Pulmonary Fibrosis (IPF) in clinical real life practice

European valorisation / extension of the cohort

Will be a key database with the ERN-LUNG European healthcare Reference Network on rare pulmonary diseases