"eurIPFreg: A European Registry and Biobank for Patients with Idiopathic Pulmonary Fibrosis"

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Giessen, Germany

On behalf of the European IPF Registry
(www.pulmonary-fibrosis.net)
Idiopathic Pulmonary Fibrosis
Why do we need an IPF Registry?

• Usually affects individuals at the age of 50 or older
• Presents with dyspnea on exertion and at rest
• IPF is **deadly**, with a median survival rate of 2-3 years.
• **Not easy to diagnose**, needs expert evaluation
• **Idiopathic** disease (cause unknown)
• **Not common** disease, many centers need to collaborate for sufficient patient numbers
• **Course** of an individual patient largely **unpredictable**
• Numerous **treatment failures**, significant side-effects with `treatment`
### Connective Tissue Diseases
- Scleroderma
- Polymyositis-Dermatomyositis
- Systemic Lupus Erythematosus
- Rheumatoid Arthritis
- Mixed Connective Tissue Disease
- Ankylosing Spondyritis

### Primary (Unclassified)
- Sarcoidosis
- Langerhans cell histiocytosis
- Amyloidosis
- Pulmonary vasculitis
- Lipoid pneumonia
- Lymphangitic carcinoma
- Bronchoalveolar carcinoma
- Pulmonary lymphoma
- Gaucher's Disease
- Niemann-Pick Disease
- Hermansky-Pudlak syndrome
- Neurofibromatosis
- Lymphangioleiomyomatosis
- Tuberous Sclerosis
- ARDS
- AIDS
- Bone Marrow Transplantation
- Postinfectious
- Eosinophilic pneumonia
- Alveolar Proteinosis
- Diffuse Alveolar Hemorrhage Syndromes
- Alveolar microlithiasis
- Metastatic calcification

### Treatment-Related / Drug-Induced
- Antibiotics – nitrofurantoin, sulfasalazine
- Antiarrhythmics – amiodarone, propanolol
- Anti-inflammatory – gold, penicillamine
- Anti-convulsants – dilantin
- Chemotherapeutic agents – bleomycin, cyclophosphamide, methotrexate, azathioprine
- Therapeutic radiation
- Oxygen toxicity
- Narcotics

### Occupational and Environmental Diseases
#### Inorganic
- Silicosis
- Asbestosis
- Hard-metal pneumoconiosis
- Coal worker’s pneumoconiosis
- Berylliosis
- Aluminum oxide fibrosis
- Talc pneumoconiosis
- Siderosis (arc welder)
- Stannosis (tin)

#### Organic
- Bird breeder’s lung
- Farmer’s lung
- Bacteria – e.g. NTB mycobacteria
- Fungi – e.g. Aspergillus
- Animal protein – e.g. Avian
- Chemical sensitizers – e.g. isocyanates

### Idiopathic Fibrotic Disorders
- Acute interstitial pneumonitis (Hamman-Rich syndrome)
- **Idiopathic Pulmonary Fibrosis**
- Familial Idiopathic Pulmonary Fibrosis
- Desquamative interstitial pneumonitis
- Respiratory bronchiolitis
- Cryptogenic organizing pneumonia
- Nonspecific interstitial pneumonitis
- Lymphocytic interstitial pneumonia (Sjögrens Syndrome, AIDS, Hashimoto’s)
- Autoimmune pulmonary fibrosis (inflammatory bowel disease, PBC, ITP, AIHA)
Natural history of IPF

- Asymptomatic period
- Lung microinjuries
- Beginning of symptoms
- Rapid progressive
- Acute exacerbations
- Slowly progressive

Survival

Years

Unknown

0
1
2
3
4
5
6
7
8
9
10

Diagnosis

Years

Unknown

0
1
2
3
4
5
6
7
8
9
10

Diagnosis

Years
Open questions

• Epithelium versus mesenchyme or both?
• Second hits: which ones, how many, how severe?
• When actually does IPF start?
• Early markers of IPF and their potential use?
• Is IPF reversible at all?
• Overlap and differences between different forms of IPF?
• Intraindividual response pattern to given treatment modalities?
How to answer these questions?
The European IPF Network: towards better care for a dreadful disease

A. Guenther* and on behalf of the European IPF Network*

Idiopathic pulmonary fibrosis (IPF) is one of the most aggressive forms of diffuse parenchymal lung disease (DPLD) and affects ~340,000 people in Europe and North America [1]. Despite extensive research over the past 25 yrs, considerable investment in controlled clinical trials, and significant progress in defining appropriate outcome measures and surrogates of disease progression, IPF remains a progressive and invariably fatal disease with a mean survival of ~3 yrs from diagnosis.

been relevant to IPF pathogenesis, such an approach might have led to rapid success, with the costs for establishing a new therapy for IPF much reduced compared with the development of completely new agents. However, in the face of many failed trials, IPF researchers working in both academia and industry are now faced with the realisation that this approach is unlikely to yield a much needed new therapy for this disease.

For many years, the arduous task of deciphering the
European IPF Network and Registry / Biobank

**European IPF network**
Natural Course, Pathomechanism and Novel Treatment Options in Idiopathic Pulmonary Fibrosis

Funded through FP7 from 01.01.08 until 30.06.11 (EU)

**European IPF Registry and Biobank**
- opened 04/09 by eurIPFnet
- open to all interested scientists

- Tight collaboration with German Center for Lung Research (DZL)
What is the European IPF Registry?

- A European database of longitudinal data from IPF patients

- Includes control groups of patients with other lung diseases

- Born out of the EU 7th Framework Programme funded project European IPF Network (eurIPFnet)
Beginnings of the Registry and Biobank

eurIPFnet members at the Kick-Off Meeting in Giessen, February 2008
Administrative Structure

Coordinator — main point of contact for outside entities

Steering Committee:
- 2 voted members from eurIPFnet +
- 2 voted members from eurIPFreg +
- Coordinator

Parties of the Consortium Agreement

Registered Site Investigators

Ethics Committee

Funding Entities

General Assembly
eurIPFreg Steering Committee

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http://www.chu-dijon.fr/...
European IPF registry

Countries contributing to eurIPFreg

Legend:
- Active sites
- Sites with pending contracts
# Data included in the European IPF Registry

**Date:** 22.01.2013 - 22:26 (MEZ)  
**Site Investigator:** Dr. med. Fotios Drakopanagiotakis  
**Project:** European IPF Network (21.01.2013 - 15:38:53 (MEZ))  
**Centre:** Giessen Lung Center  
**Country:** Germany  
**Patient:** Pat-ID: aaa000

<table>
<thead>
<tr>
<th>Planned visits</th>
<th>Baseline</th>
<th>1. Followup</th>
<th>2. Followup</th>
<th>Next visit</th>
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</thead>
<tbody>
<tr>
<td>Date</td>
<td>01.05.09</td>
<td>01.11.09</td>
<td>01.05.10</td>
<td></td>
</tr>
<tr>
<td>Data entry</td>
<td>05.06.09</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Patient’s questionnaire BASELINE**

**Patient’s questionnaire FOLLOW-UP**

**QoL questionnaires**

**Print out patients documents**

**Physician’s questionnaire BASELINE**

**Physician’s questionnaire FOLLOW-UP**

**HR-CT**

**PDF Upload**

**Biological materials**

**Final submit form for expert verification**

**Patient’s review status**

**Caserotes**
Patient’s baseline questionnaire:

- Nature and history of complaints
- Coughing and expectoration
- Concomitant complaints
- Smoking history
- Previous Airway or lung disease
- Concomitant diseases
- Medication at the time of evolution of symptoms
- Family history
- Environmental aspects
- Professional activities
- Quality of Life
  - EQ5D VAS
  - Mahler
  - SF 36
Patient’s follow-up questionnaire:

- Change of overall condition
- Infectious episodes, criteria
- Hospitalizations (duration, reasons)
- Lung transplantation status
- Professional activities
- Quality of Life
  - EQ5D VAS
  - Mahler
  - SF 36
### Histological Examination

<table>
<thead>
<tr>
<th>Description</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of marked fibrosis/architectural distortion, ± honeycombing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of patchy involvement of lung parenchyma by fibrosis</td>
<td></td>
<td></td>
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<tr>
<td>Presence of fibroblast foci</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence of marked fibrosis/architectural distortion, ± honeycombing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patchy or diffuse involvement of lung parenchyma by fibrosis, with or without interstitial inflammation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Honeycomb changes only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence of features against a diagnosis of UIP suggesting an alternate diagnosis (see below)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyaline membranes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organizing pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granulomas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marked interstitial inflammatory cell infiltrate away from honeycombing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predominant airway centered changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other features suggestive of an alternate diagnosis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 9) Echocardiography

Echocardiography results for Patient ID A2UGZ21L.
14) HR-CT results

**HR-CT performed on**

- [ ] dd.mm.yyyy

**The HRCT has been uploaded in DICOM format**

- [ ] Yes

**HRCT**

- Subpleural, basal predominance
  - [ ] Yes

- Reticular abnormality
  - [ ] Yes

- Honeycombing with or without traction bronchiectasis
  - [ ] Yes

- Upper or mid-lung predominance
  - [ ] Yes

- Peribronchovascular predominance
  - [ ] Yes

- Extensive ground glass abnormality (extent>reticular abnormality)
  - [ ] Yes

- Profuse micronodules (bilateral, predominantly upper lobes)
  - [ ] Yes

- Discrete cysts (multiple, bilateral, away from areas of honeycombing)
  - [ ] Yes

- Diffuse mosaic attenuation/air-trapping (bilateral, in three or more lobes)
  - [ ] Yes

- Consolidation in bronchopulmonary segment(s)/lobe(s)
  - [ ] Yes
Data included in the European IPF Registry

Physician's questionnaire baseline Page 4/4

20) Medical treatment for IPF

a) Anti-fibrotic medication

<table>
<thead>
<tr>
<th>Generica # 1</th>
<th>Generic name</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

To select a drug from ATC, click on the button "Catalog" and search the drug (top field in the pop-up window).

**Important**: You must select the drug in level 5 (right part of the table) by clicking the drug name or ATC. Previous level indicate only a family of drugs. Expand the following levels by clicking the arrows on the left.

**Dose**

- [ ]

**Route of administration**

- Oral
- SC
- Inhal
- IV
- TC

**x/day**

- [ ]

**Unit**

- mg
- μg
- ng
- U

**Start**

- [ ] mm/yyyy

**End**

- [ ] mm/yyyy
Data included in the European IPF Registry

Date: 01.11.2012 - 20:55 (CET)
Site: Dr. med. Fotios Drakopanagiotakis
Investigator: European IPF Network (1.40)
Project: Giessen Lung Center - IPF Patients, Germany
Centre: Germany

Patient: Pat-ID A2UGZ21L
Baseline: 01.11.2012 (CET)
Form: Physician's questionnaire
family: BASELINE
Form: *medical treatment

d) Side Effects

Side Effects 1
Catalog | Side effect
---|---

Catalog | Generica

Comment

Delete
More
bio sample

Bio sample #

Bio sample # 1

Date of sampling: dd.mm.yyyy
LabID (do not edit): 8m8iro
Type of specimen: Please choose
Date of receipt of sample (to be filled out later): dd.mm.yyyy

histslides

Upload an image

Upload an image

Upload an image

Upload an image

Upload an image

Upload an image

Upload an image

Upload an image

Delete

More

Cancel  Save  Check data
Research in eurIPFreg

„bottom up“
from the test tube to humans

Clinical Trials
Patient Biomaterials
Pharmacology
Animal experiment
Cell culture
Molecular biology
Protein / Lipid chemistry

„top down“
from humans to the cell / animals

Clinical Observations
Human Biomaterial
~omics, NGS
Pathomechanistic concept
gain-of-function
loss-of-function
in vitro/vivo
European IPF registry

Multi-level
Informed
Consent
Procedure

I hereby declare that I am taking part in the above-mentioned trial/the above-mentioned research project. I have been advised that my participation in the trial/research project is voluntary, that I do not incur any disadvantages by refusing to participate and that I have the right to stop my participation at any time, without giving reasons.

I agree to the collection, storage, processing and transmission of information on my health and biological materials within the context of the trial “European IPF Register” described in the Patient Information.

I also agree that authorized employees of the domestic and foreign supervisory authorities and of the sponsor may have access to my personal data in the course of their duties for monitoring purposes. These persons are bound by a duty of confidentiality. I have been informed of my data protection rights.

__________________________  ____________________________  ___________________________
<Place>  <Date>  <Patient>

I hereby expressly declare that I transfer to the European IPF Register all rights of ownership of all biological materials already previously collected by the doctors treating me, ____________________________ (names) and, further, all rights of ownership of the biological materials to be collected in the future by the doctor obtaining my informed consent for this trial.

Yes ( )  No ( )

Irrespective of my basic participation in the trial, I agree to the performance of genetic tests on the biological materials obtained from me.

Yes ( )  No ( )

I hereby expressly declare my wish to be informed in a suitable way about knowledge obtained from any new and relevant genetic tests of my biological materials.

Yes ( )  No ( )

I hereby expressly declare my wish to be informed about clinical trials investigating the safety and/or efficacy of certain drugs, for which I could, in principle, be considered, on the basis of the status of my disease.

Yes ( )  No ( )

I also wish to be informed about new knowledge obtained in the context of the research activities of the European IPF Register, if these have been obtained from my biological materials and permit conclusions about the further course of my disease.

Yes ( )  No ( )

__________________________  ____________________________  ___________________________
<Place>  <Date>  <Patient>

__________________________  ____________________________  ___________________________
<Place>  <Date>  <Informing doctor>
Patient recruitment in the eurIPFreg (only IPF)
Publications resulting from the work of

**Conte E, et al. Lab Invest. 2013 May;93(5):566-76
**Nkyimben T, et al. PLoS One. Accepted for publication July 2013

** indicates joint publication of consortium members
Visibility of the Registry

Editorial

The European IPF Network: towards better care for a dreadful disease

For more information visit www.pulmonary-fibrosis.net

Europeans respiratory society - every breath counts

European Respiratory Society - All rights reserved
www.ersnet.org
Research goals of the European IPF Registry

• a) Future development of non-invasive, air- or blood-borne biomarkers in IPF allowing safe diagnosis, sub-grouping of IPF subjects and identification of therapy-responders

• b) Quality of Life assessment

• c) Description of epigenetic changes in IPF lung epithelial cells and fibroblasts

• d) Genome profiling in IPF subjects

• e) Isolation of progenitor cells and different parenchymal cell populations from IPF and other lungs
PATIENTS

- eurlIPFreg Coordinator (Andreas Guenther)
- eurlIPFreg Steering Committee
- Physicians and nurses providing clinical care
- UKGM-TransMIT
- Industry
- Scientists involved in IPF research
- External Site Investigators
- Scientific Collaborators and Advisors
- Staff of the eurlIPFreg (Sabine Heinemann, Stefan Kuhn, Bettina Paul, Conny Scheld)
- eurlIPFreg Project manager (Sandy Jones)
Thank you!