EMPIRE

European MultiPartner Ipf Registry

PROTOCOL

Approved by	Date	Name/ Signature
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MUNI MED Institute of Biostatistics and Analyses

EMPIRE (IPF)

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PROTOCOL

version 2.0

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1 SUMMARY INFORMATION

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Project summary		
Project title		European MultiPartner IPF Registry
Project short name		EMPIRE
Expected duration of project		Not available
Project number		IBA0866
Guarantor	**Name and Surname**	Prof. Martina Vašáková, M.D., Ph.D.
	Clinic/ Department	Department of Pulmonary Medicine
	Hospital	Thomayer Hospital
	Country	Czech Republic
IBA FM MU	**Title**	Institute of Biostatistics and Analyses at the Faculty of Medicine of the Masaryk University, Brno, Czech Republic
	Residence	Kamenice 5, 625 00 Brno, Czech Republic
	Project manager	Filip Kňažek, M. Sc.
Language		English
Characteristics of the patient population		Patients diagnosed with idiopathic pulmonary fibrosis according to ATS (American Thoracic Society) / ERS (European Respiratory Society) / JRS (Japanese Respiratory Society) / ALAT (Latin American Thoracic Association) statement.
Protocol	**Date of protocol**	01 July 2018
	Version of protocol	2.0.
	Number of appendices and date	2

1.1 List of abbreviation

ADR	Adverse Drug Reaction
AE	Adverse Event
ALAT	Latin American Thoracic Association
ATS	American Thoracic Society
CRF	Case report form
EC	Ethics Committee
eCRF	Electronic case report form (data forms)
ERS	European Respiratory Society
FVC	Forced vital capacity
HRCT	High-resolution computed tomography
IBA	Institute of Biostatistics and Analyses
IBA FM MU	Institute of Biostatistics and Analyses at the Faculty of Medicine, Masaryk University
ID	Identification number
IPF	Idiopathic pulmonary fibrosis
JRS	Japanese Respiratory Society
SUKL	State Office for Drug Control
TLCO	The transfer factor for carbon monoxide
UIP	Usual interstitial pneumonia

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2 INTRODUCTION

Idiopathic pulmonary fibrosis is defined as a specific form of chronic fibrosing interstitial pneumonia which affects exclusively lung parenchyma. The key characteristics of the disease involve the exclusion of all other causes of interstitial lung disease, radiological pattern of usual interstitial pneumonia (UIP) documented by high-resolution computed tomography (HRCT), and histological findings of UIP (13). To establish the IPF diagnosis, ERS/ATS/JRS/ALAT criteria have been adopted (6). Although it is generally assumed that IPF is a relatively rare disease, the most recent studies on this topic suggest that the incidence might be significantly higher (13).

2.1 Type of study:

The project is an international, multicenter, observational, prospective, non-interventional registry of IPF patients in the Czech Republic, Central, and Eastern Europe. Patients treated by all available treatment modalities will be included in the registry.

3 OUTCOMES OF THE PROJECT

3.1 Primary outcome

- To estimate IPF incidence, prevalence and mortality (biennial and in general) in Central and Eastern Europe

3.2 Secondary outcome

- To describe basic characteristics (e.g. age, gender, risk factors etc.) of patients with IPF

3.3 Tertiary outcome

- To describe real life approach to IPF in participating countries from Central and Eastern Europe:
  - diagnostic algorithm
  - treatment patterns and management of patients with idiopathic pulmonary fibrosis
  - treatment outcomes (treatment response, overall survival) and quality of life
  - resource utilization
- To determine number of patients suitable for enrolment in clinical trials

3.4 Endpoints

- FVC decrease, TLCO decrease, death

4 PROJECT DESIGN

4.1 Overall study design

The EMPIRE IPF registry is a prospective, international, multicenter, observational, non-interventional, open-label, non-randomized registry of adult IPF patients. Patients treated by all available treatment modalities will be included in the registry.

Data collection starts with the registry initiation after local approval according to national regulations.

Data about each patient will be collected prospectively from the time of enrolment and subsequently every 3 or 6 months, until the patient's death or lung transplantation (as defined in the registry

structure). The frequency of the follow up visits will be at the discretion of the treating physician and must follow standard clinical practice of each centre.

Following data will be collected: patients' characteristics and medical history, diagnosis and disease management, resource utilization, treatment outcomes, quality of life (will be assessed using EuroQoL questionnaire).

Enrolment in each part will be determined only by diagnosis of IPF as per physician assessment and will not be dependent on the treatment choice.

Safety reporting for patients treated with individual drugs will follow standards of companies that support the registry or supply the individual drugs. Data will be collected via electronic data forms (eCRFs).

4.1.1 Inclusion criteria

- Confirmed diagnosis of idiopathic pulmonary fibrosis (IPF)
- Signed Patient´s informed consent

4.1.2 Exclusion criteria

- Patient is not able or willing to participate. However, demographic data will be collected (age, gender) to obtain incidence and prevalence data.

4.2 Observed population

All patients with a confirmed diagnosis of idiopathic pulmonary fibrosis based on ERS/ATS/JRS/ALAT criteria will be enrolled into the study following their consent. No other inclusion criteria will be applied.

4.3 Participating countries and sites

Tab. 1 Participating centres in the Czech Republic

No.	City	Centre
1.	Prague	Thomayer Hospital, Department of Pulmonary Medicine + General University Hospital in Prague, Department of Tuberculosis and Respiratory Diseases + Hospital Na Bulovce, Department of Pulmonary Medicine and Thoracic Surgery
2.	Prague	University Hospital in Motol, Department of Pulmonary Medicine
3.	Plzeň	University Hospital Plzen, Department of Tuberculosis and Respiratory Diseases
4.	Hradec Králové Pardubice	University Hospital Hradec Kralove, Department of Pulmonary Medicine Regional Hospital Pardubice, Department of Pulmonary Diseases and Tuberculosis
5.	Olomouc Kroměříž	University Hospital Olomouc, Department of Pulmonary Diseases and Tuberculosis + Hospital in Kromeriz, Department of Pulmonary Medicine and Allergology
6.	Brno Znojmo Jihlava	University Hospital Brno, Department of Pulmonary Diseases and Tuberculosis + Hospital Znojmo, Department of Pulmonary Medicine + Hospital Jihlava, Department of Pulmonary Medicine

7.	Ústí nad Labem	Regional Medical Association, JSC - Masaryk Hospital in Usti nad Labem, Department of Pulmonary Medicine
8.	České Budějovice	Hospital Ceske Budejovice, JSC, Department of Pulmonary Medicine and Tuberculosis
9.	Ostrava Nový Jičín	University Hospital Ostrava, Department of Tuberculosis and Respiratory Diseases + Hospital Novy Jicin, Department of Pulmonary Medicine
10.	Zlín	Tomas Bata Regional Hospital, JSC, Department of Pulmonary Medicine

The EMPIRE registry is organized in a several countries. Project started as the Czech registry of IPF, then several countries of Central and Eastern Europe joined the registry. Currently the study is organized in these countries: Czech Republic, Slovakia, Hungary, Poland, Serbia, Croatia, Turkey, Israel and Bulgaria. Some more countries will be joining the registry. Updated status of currently involved countries is available on the project website: http://empire.registry.cz/index-en.php?pg=participating-centres

4.4 Participation and completion of the registry

From the moment of provision of an informed consent, the patient is considered to be a participant in this project. All national rules and regulations will be respected. Patients will be treated according to standard clinical practice, without being affected by their participation in this project. Data and results will be collected anonymously. All participating patients must be informed about the project in their mother tongue before any information is collected. The investigator must document that he provided the patient with adequate information. If the patient refuses to participate, just the demographic data will be collected to assess the potential selection bias.

5 METHODOLOGY

5.1 Collected data

Patients treated by all available treatment modalities will be included in the registry. The registry database will include patient forms as indicated below.

5.1.1 Entry form

- Basic record
- Diagnosis
- Clinical signs
- Medication
- Associated disorders (comorbidities)

5.1.2 IPF Treatment

- Specification of treatment/medication
- Clinical trials-participation
- Rehabilitation

- Long-term oxygen therapy
- Lung transplantation

5.1.3 Follow up Form

- Lung function tests
- Results of Spiro-Ergometry/ 6MWT
- High-Resolution Chest CT
- Subjective state (NYHA)
- Pulmonary Hypertension
- New associated disorders and complications
- Lung transplantation
- Current status of the patient

5.1.4 Quality of life

- Quality of life Form (EuroQoL or f)

5.1.5 Hospitalization since last visit

- Duration of hospitalization

5.1.6 End of observation

- End of observation (reasons)
- Date of death
- Cause of death
- Date of last contact

5.1.7 Adverse Event form

- Administered drug
- Date
- Type of AE
- Severity
- Assessment of AE

6 STEERING COMMITTEE

The Steering Committee has the overall responsibility for the conduct of the study according to Good Clinical Practice as well as all applicable requirements imposed by the reviewing Ethics Committee. For this study, the Steering Committee will have certain direct responsibilities and will delegate other responsibilities to appropriate consultants or to IBA FM MU. Together, Steering Committee, consultants and IBA FM MU will ensure that the study is conducted according to the study protocol and all applicable regulations. All personnel to participate in the conduct of this clinical trial will be qualified by education and/or experience to perform their tasks.

Steering Committee members are the leaders of respective countries who have confirmed their willingness to be part of the registry and enroll patients according to the Protocol. The leaders are also responsible for ensuring the submission to the regulatory authority, with IBA FM MU support if needed. Steering Committee members shall participate in the face to face and teleconference Steering Committee meetings, lectures on specific topics, taking the role of national coordinators in their respective countries, publishing of scientific data from the EMPIRE project, giving scientific advice etc.

7 DATA ANALYSIS

7.1 Statistical analytical plan

Statistical analytical plan was not prepared.

7.2 Statistical methodology of data processing

Data management and statistical analysis is done by Institute of Biostatistics and Analyses at the Faculty of Medicine, Masaryk University Brno, Czech Republic.

Data from both incident and prevalent cases will be collected. Statistical analyses will be descriptive to reflect the project designed (an observational, non-interventional). No formal hypothesis will be tested.

Basic description of patient cohorts and monitored parameters will be performed by means of frequency tables and descriptive statistics: mean, standard deviation, median, minimum, and maximum. All estimates will be accompanied with 95% confidence intervals. Incidence of patients will be expressed as the overall number of newly diagnosed patients as well as the number of new cases per 100,000 people at risk. Similarly, prevalence of patients with IPF will be given in absolute number as well as the number of living patients per 100,000 people at risk at the same time.

Treatment modalities in time by stage of disease will be presented. Moreover, the type and frequency with which various treatments and treatment combinations are used will be summarized by line of therapy. For all IPF therapies additional summary of treatment duration will be presented. Changing patterns of treatment over time will be also considered. Treatment groups will be stratified by patient participation in randomized – controlled studies.

The new drug user design will be followed – newly diagnosed treatment naïve patients are to be analysed as well as patients already treated. Standard Kaplan-Meier approach will be adopted for the visualization of survival data and supplemented by median survival and/or survival in defined time points; all survival descriptive statistics will be supplemented by its 95% confidence intervals.

Statistical analysis will be carried out using Statistica for Windows 12.0 (Statsoft, Inc.), and SPSS 22.0.0 (IBM Corporation).

7.3 Plan of analyses

The summary report of whole EMPIRE registry is prepared once a year, as well as national reports (data analysis for each country). Data export are prepared twice a year, usually January and July, and during this period, all data are analyzed based on given data export.

During the run of the registry Investigator Initiated Study appears to test the hypothesis based on EMPIRE data.

8 REGULATORY AND LEGISLATIVE REQUIREMENTS

In accordance with valid rules, the following is applied:

Purchaser and database owner is MU. Institute of biostatistics and analyses FM MU administrates the database. Purchaser and database owner guarantee IT facilities and is the processor of the database. Primary data (ie. Patient data) are data processed by individual centres (usually medical facilities).

The main project guarantee is: Prof. Martina Vašáková, M.D., Ph.D.

Detailed information on setting up the project, the role of the professional guarantor and the IBA FM MU are described in the Art. 9 and in the Appendix 1 to the protocol: Ensuring professional guarantees, roles and processes in the operation of clinical registries and databases for the study of European MultiPartner IPF Registry.

8.1 Informed Consent Form

The reviewing Ethics Committee (EC) must review and approve an informed consent (ICF) specific to this study. IBA FM MU will provide each study centre with an example ICF in English language. Each centre has an obligation to have the ICF translated into their local language. One translation for a country is enough. The centre has to have a certificate of the translation. The study centre, to meet specific requirements, may modify English example ICF; however, the ICF to be used for patient consent under this protocol must contain all elements required by the protocol. The original, signed and dated ICF must be retained by the investigational site for monitoring, and a copy provided to the subject.

8.2 Ethics Committee approval

The IPF EMPIRE registry study will be submitted to Iocal EC in each participating country prior the project initiation.

8.3 Regulatory requirements

The project is registered in the Czech Republic from SUKL as a non-interventional registry. Under an identified number 1412080000.

8.3.1 Personal Data Protection

The processing of personal data of natural persons involved in the registry is carried out in accordance with the requirements and provisions of Act No 101/2000 Coll, On the protection of personal data and on Amendments to certain Acts, as amended or with legal regulation replacing this Act, and in accordance with Regulation (EU) 2016/679 of the European parliament and of the Council on protection of nature persons with regard to the processing of personal data and on the free movement of such data (hereinafter „GDPR"). Both the controller and the processor are obliged to observe the rules and obligations coming from GDPR, as well as to set up the relevant processes for data subjects rights fulfilment.

Whether personal / pseudonymous or anonymous data is processed within the registry, it is always a protected information processing.

8.3.2 Patients' Personal Data Processing

The Controller of personal data, who determines the purposes and means of processing within the study/register is Masaryk University, Faculty of Medicine, with registered office in Žerotínovo nám. 617/9, 601 77 Brno, Czech Republic and its principal place of business at the Kamenice 126/5, 625 00 Brno, Czech Republic. (hereinafter only as „IBA FM MU").

The patient can´t be included to the project without signed **explicit informed consent**. Acquirement and storage of patient informed consent for statistical and scientific purposes is responsibility of the Provider of health services (centre) according to conditions stated in the contract. The exact purposes are described at the informed consent form, which is the appendix No. 2 of this document. The information, that the patient has given the consent with processing of his/her data should be confirmed at EDC system for data collecting. Without this confirmation, new patient can´t be added.

The investigator/ health care facility is not a controller of the data for the purpose of the registry. The physician shall enter patient´s data into the registry under a unique ID, the attending physician is the only person who can identify the patients based on the ID. Other persons accessing the registry/study are unable to identify a patient in the register. The patients are informed about their rights within the informed consent. Patients can apply their rights directly at the office their attending physician. The physician shall be familiarized with rules for personal data processing in the form of binding standard procedure provided by controller so IBA FM MU.

8.3.3 Investigators´ Personal Data Processing

Within the registry the personal data of cooperating investigators are processed by IBA FM MU on base of cooperation agreement for purposes the entering of data into the registry, the creation of access accounts and the payment of remuneration for work. On the base of legitimate purpose of the controller the contact investigator data are processed for ensuring of smooth running of the register and high quality of collected data.

The investigators are properly informed about processing of their data.

8.3.4 Ensuring of Personal Data Protection

IBA FM MU has implemented the following measures in compliance with the ethical and legal requirements to ensure the maximal possible safety of collected data:

- Technical measures of EDC system
- Internal standards form personal data processing, risks management, incident management, training system
- Access policy – access to the data only for authorized person on the base their access rights

9 TRAINING OF INVESTIGATORS CONFIDENTIALITY

All patients will be assigned unique ID. Identification of any patient from the unique ID will not be possible. Verification of the source data will not be performed. The identity of a patient behind the unique ID number is known only to the provider of healthcare.

9.1 Description of the measures taken to protect data

Data stored in the database are pseudonymised, information regarding treatment is stored under IDs that do not allow identification of natural person. All data transfers are encrypted and their possible misuse during transmission is avoided.

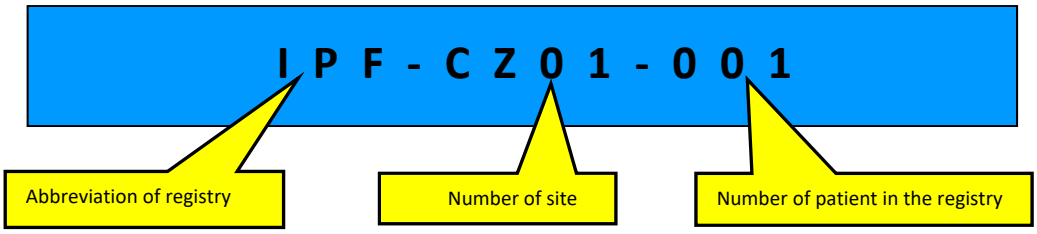
Order of patients enrolled in each centre is generated automatically. The patient' ID is generated in the prescribed form: **IPF-AA01-001** (see below),

IPF – abbreviation of the registry EMPIRE

AA01 – Number of site – for each country relevant prefix

001 – Consequent number of patient in the registry

Figure 1: Diagram of generated ID



9.2 Archiving and manipulation with documents

The documentation of individual cases (ie information regarding treatment of a patient) will be archived by the healthcare provider (centre) according to applicable regulations and legal regulations. Anonymized/pseudonymised data in the registry. Data will be disposed of at the request of the centre that generated the data.

9.3 Possible sharing of data

Primary data ie. data generated by individual centre, will not be shared with any entity, not even the other centre. **Secondary data,** ie. results of statistical analyses performed by IBA FM MU will be available to other centres. The secondary data is the intellectual property of IBA FM MU, however, they can be published or be available of tertiary sites with the agreement of scientific leader of the project in a respective

y or Steering Committee approval.

10 PHARMACOVIGILANCE

Should any Adverse Event or Adverse Drug Reaction be reported during the study, this must be reported to the database via electronic form included in the CRF. **The reporting of records through e-form will generate an e-mail in the form of an Adverse Event message sent immediately after filling the pre-defined fields in the e-form. What type of event must be collected is managed according to contracts between IBA and involved pharma companies.** The investigators' responsibility for pharmacovigilance reporting to respective Health Authorities in particular country remains intact.

11 TRAINING OF CENTRES AND STARTING OF DATA COLLECTION

The EMPIRE project was launched in 2014, based on the Czech IPF registry, which was initiated in 2012. The project started in three another countries – Slovakia, Poland, and Hungary. During the Registry operation, some more countries joined the Registry and it can be expected to engage further countries.

A technical manual about data entry and working with software was prepared, as well as clinical manual how to deal with validation of the system.

New sites will obtaine prepared manuals and can ask for training through teleconference devices (WebEx).

12 PUBLICATION RULES

General rules for publishing are included in Appendix 1 to this protocol.

13 BUDGET OF STUDY

The budget of study is a separate document, which is not published, nor distributed together with the protocol.

13.1 Preliminary calculation of budget

Preliminary calculations in a more detailed breakdown for the first period of the study, starting from the date of commencement by 31 December of the first calendar year, is a part of separate documentation which is not published together with the protocol. The calculation for subsequent years will be updated every December of the given calendar year.

14 SCHEDULE

14.1 Data collection schedule

Data are collected continuously and are updated every 3 or 6 months if possible.

Data on each patient are collected from the time of enrolment and subsequently every 3 or 6 months, until the patient's death or lung transplantation (as defined in the registry structure).

The data about each patient are collected prospectively from the time of enrolment and subsequently, usually every 3 or 6 months. The frequency of the follow up visits will be at the discretion of the treating physician and must follow standard clinical practice of each centre.

Tab. 2 Data collection time points

MONTH/DATE	DATA COLLECTED
0m	Entry form, Treatment
Every 3m/6m	Treatment, Follow-up Information, Quality of life form, Hospitalization, Adverse Event form (if AE occurred)
End of observation	End of observation

14.2 Project schedule/timeliness

The data collecting was initiated in 2014. The collecting of data is continuously and long-term. The term for project completion was not set up and it is expected to run long-term.

15 QUALITY ASSURANCE AND CONTROL

Qualified personnel will perform data entry in an electronic CRF (eCRF). Data entry and verification will be handled according to the applicable data handling procedures.

All eCRF pages will be subject to initial inspection for omitted data, gross data inconsistencies, illegible data and deviations by the IBA FM MU before the statistical analysis. Any deficiencies or deviations will be reviewed and any necessary action determined (e.g., data query, communication to the study centre). Intermittent data review (including crosschecks) will be performed and any discovered errors

will be reported to the study site using the data correction and query process (as necessary). The study site will be expected to review the query, make any necessary corrections or comments, and return to data management where the correct response will be entered into the database.

16 INSURANCE

Not applicable.

17 REFERENCES

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Appendix No. 1 to the Protocol, ver. 2.0

Ensuring professional guarantees, roles and processes in the operation of clinical registries and databases for the study of European MultiPartner IPF Registry

A. Basic Provisions

1. These rules apply solely to non-interventional clinical research projects, especially retrospectively collected data in diagnostic and clinical databases and observational studies.
2. The project is headed by the Steering Committee, composed of representatives of all participating countries. A representative of a participating country (usually the head of the biggest or initiating workplace in given country qualified person) becomes a member of the Steering Committee no later than upon the commencement of the collection of data from the given country/workplace.
3. Representatives of the centres act in the position of investigators/data managers within projects, i.e. persons responsible for the accuracy of data entered.
4. The Steering Committee is headed by the Principal investigator of the project (head of the Steering Committee), who is elected by the members of the Steering Committee. Head of the Steering Committee is an important scientific personality capable of identifying and promoting the strategic objectives of the project and raising funds for them. The Principal investigator's task is primarily to coordinate and manage the project as a whole; the use of the data collected in the registry for any purpose must always be approved by the Steering Committee of the project.
5. Clinical registries and observational studies only collect pseudonymised and anonymised data that does not allow any direct or indirect identification of the patient. Members of the project team are not permitted to identify the identity of persons. The only person or entity that has the potential capability to identify the patient/data subject is the person or entity that entered the data into the registry.
6. The registry (primary database of the project) collects pseudonymised data that are subsequently anonymised for further scientific analysis. Since the pseudonymised data are considered to be personal data, the project management must be adapted in accordance with applicable legislation, including informed consents of the data subjects. The informed consent of the subject must clearly indicate that the subject has received information that some of the subject's data will be entered into the registry (albeit in anonymised or pseudnonimised form) and processed in the Registry operated by Masaryk University.
7. The registry itself, database and software tools, including software for reporting or on-line reporting, are the intellectual property of Masaryk University (MU) as the project operator and IT guarantee. Representatives of centres or investigators may be co-authors in the development of the relevant tools. Unless expressly agreed otherwise, Masaryk University is the producer of the database.
8. Within the projects, IT tools and services are covered in the form of jointly received grants, donations or sponsorships; they are not charged to individual centres or hospitals. The access of centres to these tools and services is equal and does not depend on the number of their records in the database.
9. The producer of the database and project IT facilities within the meaning of paragraph 7 is Masaryk University.
10. Data collected in the databases of clinical registries and observational studies is seen in the project as part of the medical records of individual clinical centres. These centres are

therefore the administrator and holder of primary data; MU acts as a data processor. Primary data may be handled only with the explicit consent of all centres. Secondary data (i.e. information that MU obtains by statistical processing of primary data) will not be published or commercially exploited without the consent of individual centres. The rules set out in Sections B and C must be followed.

B. Rules of professional guarantee, securing and operational of projects

1. The technological solution and settings of ICT tools for the project are based on the approval and decision of the project's Steering Committee. The producer and provider of the technological solution are the Institute of Biostatistics and Analyses at the Faculty of Medicine, Masaryk University (from now on referred to as IBA FM MU).
2. The data entered by healthcare facilities is centralized on IBA FM MU servers. The IBA FM MU is obliged to provide the necessary security facilities. Depending on the circumstances, separate agreements between the Faculty of Medicine of Masaryk University and individual healthcare facilities regarding the security and operational aspects of their cooperation may be concluded. IBA FM MU always offers parallel localization to the centres of data entered by them in the local database kept by the relevant clinical workplace.
3. The participating clinical centre has unlimited access to its data throughout the project and may archive it in parallel in their local databases. Clinical centres have the right to withdraw from the project at any time.
4. IBA FM MU must ensure that the records of the clinical centres cannot be reviewed mutually by the parties. Each investigator has full access only to their own data, except for the leading expert guarantee who can review data of all participating centres and individual members of the Steering Committee who can review data of participating centres in given country. In addition to participating centres and IBA FM MU, no other entity has access to the project data.
5. The use of overall project data is conditional upon approval of the leading expert guarantee and members of the Steering Committee (individual clinical centres do not provide the consent). The outputs on the country level, the approval of a member of the Steering Committee of given country and further the approval of participating clinical centres in the given country is required.
6. Entries in the project databases can only be used for analyses that have been duly approved. Specifically, there are the following modes of analysis and output preparation:
    - Joint outputs of the project as a whole. The Steering Committee decides on joint outputs and they are subject to approval by the leading expert guarantee of the project and approval of each member in the Steering Committee.
    - Joint outputs on the country level. Outputs are decided by a member of the Steering Committee of given country, but any clinical centre of given country can submit a proposal for data output. The outputs are conditional upon the approval of a member of Steering Committee in the given country and with the express consent of the participating clinical centres.
    - Data analysis for individual centres. At centres level, analysis will not be processed. Clinical centre may request data export to be provided to them.
7. No analyses or summaries of internal data of the project may be carried out and presented without the express approval of the member of Steering Committee in one of the operating modes specified in the previous paragraph.
8. Representatives of the individual centres may make suggestions for certain analyses, and scientific or presentation outputs. Applications must be submitted to the Leading expert guarantee of the project who will have them discussed by the Steering Committee.
9. Primary project data must not be published or used for presentations. All outputs refer to processed, aggregated data.

10. A professional association operating in the area of the primary project objectives may provide professional patronage for the project and may express its opinions through the Leading expert guarantee of the project.

C. Procedures for the use of data in registries and observational studies, rules of communication

1. The organisation of project assumes that the common agenda and processing of applications are carried out during the Steering Committee meetings, in urgent matters also electronically or using video conferencing. The project's Steering Committee meets on regular basis for a meeting in person twice a year.
2. Suggestions for the use of project data and processing specific analyses may be submitted by any representative of the participating centres, a member of a professional association or an independent expert or expert team. Suggestions may come from outside the participating centres. Data from the project may be, with the consent of representatives of the centres, used for any form of academic and scientific work, especially conference presentations, posters, publications in domestic and foreign press, or electronic publications. Private companies, government authorities and health insurance companies may also request an analysis, for example for the purposes of obtaining population and regional data on a medicinal product. The content and scope of such a requested analysis (hereinafter referred to as the "output") must be in accordance with the report of the relevant project and must be justified by the requirements of administrative proceedings or inspection activities concerning the health services provided. The applicant or initiator of a specific output shall submit a brief written application to the Leading expert guarantee of the project, containing in particular:
    - Type of planned output and its purpose
    - Preliminary title of the final output
    - Hypothesis, specification of the analysis with defined group of patients, parameters, time intervals, groups, range of data etc.
    - Proposal for the main author of the work
    - Proposed forms of output (internal report, public publication, presentation,...).
3. The Leading expert guarantee of the project will ensure that the application will be discussed by members of the Steering Committee and delivers the final opinion to the applicant. Consent of members can be arranged through the "e-voting" feature that is part of the Registry. The Member of the Steering Committee shall then express agreement/disagreement with the provision of the data for the discussed purpose.
4. With this permission, the "applicant" officially asks IBA FM MU for an analysis; the output must be always available to the Leading expert guarantee and to all members of the Steering Committee who can then hand over the outputs to the clinical centres in the given country.
5. The actual processing of project data and publication of the project outputs are regulated by the agreed project protocol as well as by the usual rules for the proper publication of scientific results (professional opposition, approval of all co-authors, etc.).
6. The first author of the publication or scientific result is the initiator or the applicant of the output, then the authors are listed by the number of patients, then the responsible member of IBA FM MU and the last given is senior.
7. If any of the members of Steering Committee expresses disagreement in the vote, this does not automatically imply the veto of the intent. In these cases, the Steering Committee will meet via teleconference and discuss the intentions with all members again. Strategic intentions allow the approval of an absolute majority of members of the Steering Committee

INFORMOVANÝ SOUHLAS PACIENTA

s registrací klinických údajů v registru Idiopatické plicní fibrózy (EMPIRE)

Povaha a účel registru Idiopatické plicní fibrózy - European MultiPartner IPF REgistry

Registr **EMPIRE (European MultiPartner IPF REgistry)** vznikl v roce 2014 na základě databáze registru IPF (od roku 2012) jako neintervenční mezinárodní multicentrická databáze pacientů s diagnózou idiopatické plicní fibrózy (IPF) v centrální a východní Evropě. Cílem registru je hodnocení incidence, prevalence a úmrtnosti idiopatické plicní fibrózy v regionu střední a východní Evropy a stanovení základních charakteristik pacientů s touto diagnózou. Cenným údajem, sledovaným v rámci registru, jsou informace o léčbě pacientů v rámci daného regionu.

Registr EMPIRE vede Masarykova univerzita (Sídlo: Žerotínovo nám. 617/9, 601 77 Brno IČ: 00216224) pod záštitou České pneumologické a ftizeologické společnosti ČLS JEP. Jsou v něm sledovány výsledky diagnostických vyšetření, informace o léčbě a dále průběžné informace o zdravotním stavu pacientů trpících Idiopatickou plicní fibrózou. Smyslem registru je souhrnné vědecké hodnocení údajů u velké skupiny pacientů s idiopatickou plicní fibrózou. Účelem registru je nashromáždění co největšího množství dat týkající se léčby Idiopatické plicní fibrózy a následná podrobná vědecká analýza dat.

Registr EMPIRE je a nadále bude platformou pro zavádění vysoce inovativních léčebných přípravků do léčby IPF a následnou kontrolu jejich efektivity. Data z registru jsou vysoce cenná pro screening náboru do nových klinických studií s léčivy pro IPF díky jasně stanovenému poolu cílových pacientů. Data budou také následně využitelná pro farmaceutické společnosti i plátce. V neposlední řadě lze v rámci registru realizovat i tzv. investigátorem (lékařem) iniciované studie, které jsou jedinečnou platformou pro klinický výzkum této nemoci.

Primární cíl výzkumu

- Odhad incidence, prevalence a mortality (dvouleté a celkové) IPF ve střední a východní Evropě

Sekundární cíl výzkumu:

- Popis základních charakteristik (např. věk, pohlaví, rizikové faktory apod.) pacientů s IPF

Terciární cíle výzkumu:

- Popis reálné klinické praxe u IPF v zúčastněných zemích střední a východní Evropy:
  - Diagnostický algoritmus
  - Způsoby léčby a management pacientů s IPF
  - Výsledky léčby (odpověď na léčbu, celkové přežití) a kvalita života
  - Využití zdrojů
- Stanovení počtu pacientů vhodných pro nábor do klinických studií.

Rozsah sbíraných údajů a doba zpracování

Registr předpokládá sběr klinických údajů ze zdravotnické dokumentace, která je vedena poskytovatelem zdravotních služeb v souvislosti onemocněním Idiopatické plicní fibrózy. V registru se dále u jednotlivých pacientů eviduje jejich pohlaví, výška, váha, celý datum narození, iniciály, rasa, zdravotní pojišťovna a jméno ošetřujícího lékaře .

Případné výsledky projektu budou uveřejňovány pouze souhrnně, pro velké skupiny pacientů, nikoli konkrétně pro jednotlivé pacienty. Totožnost pacienta nebude nikdy zveřejněna ani postoupena mimo poskytovatele zdravotních služeb.

Jedná se o dlouhodobý retrospektivní registr. Lze očekávat, že data budou sbírána a zpracovávána dlouhodobě, v horizontu desítek let. Přesný konec sběru dat nelze v dané chvíli určit. Data, která přestanou být relevantní pro výzkum, budou neprodleně smazána. Data zůstávají uložena v registru v nezměněné podobě po dobu 15 let od ukončení registru, identifikační klíč, podle něhož je možné

určit konkrétního pacienta poskytovatel zdravotních služeb zlikviduje do jednoho roku po ukončení registru.

Garance ochrany práv pacienta

V rámci sběru údajů do registru nejsou prováděna žádná vyšetření navíc a nejsou používány žádné nové nevyzkoušené léky. Zpětný sběr dat o průběhu léčby pacienta nijak neovlivní způsob jeho léčby.

Přístup do elektronického systému registru není veřejný, je umožněn pouze správci a v omezeném rozsahu příslušnému lékaři v rámci zadávání zpracovávaných dat, a to na základě přidělených přístupových práv.

Data jsou zpracovávána pouze na základě souhlasu pacienta s jejich zpracováním.

Souhlas pacienta se zpracováním osobních údajů

Registr obsahuje výhradně pseudonymizovaná a anonymizovaná data, která jsou dobře chráněná proti zneužití. Data o průběhu léčby nejsou nikdy zpracována bez souhlasu pacienta. Proto si Vás dovolujeme požádat o poskytnutí písemného souhlasu se sběrem a zpracováváním výše uvedených údajů o Vaší léčbě pro výzkumné účely. Souhlas je dobrovolný a jeho neudělení nemá vliv na poskytovanou léčebnou péči. Souhlas můžete kdykoliv bez udání důvodu odvolat a data o vaší léčbě budou z registru vymazána.

Svým podpisem níže potvrdíte svůj souhlas, aby Váš poskytovatel zdravotních služeb (zdravotnické zařízení) zadal relevantní údaje o průběhu Vaší léčby do centrálního registru Idiopatické plicní fibrózy (EMPIRE) a k tomu, aby Masarykova univerzita (MU) tyto údaje dále zpracovávala za účelem výzkumu Idiopatické plicní fibrózy. Masarykova univerzita je správcem všech dat v registru. Vaše data nebudou předávána žádné další osobě.

Masarykova univerzita i poskytovatelé zdravotních služeb respektují přísná pravidla ochrany osobních dat (v ČR v souladu se zákonem č. 101/2000 Sb. o ochraně osobních údajů a Obecným nařízením o ochraně osobních údajů).

Masarykově univerzitě jsou údaje o léčbě pacientů předávány bez identifikačních údajů daného pacienta pod kódem, který není Masarykova univerzita schopna dešifrovat. Pacienta může ve výjimečných případech identifikovat poskytovatel zdravotních služeb. Může tak učinit pouze v případech odůvodnitelných pro zachování bezpečnosti pacienta. Identifikační údaje pacienta však ani v těchto závažných případech neopustí zdravotnické zařízení a identita pacienta pod kódem nebude Masarykově univerzitě odhalena.

Šifrování neovlivní schopnost poskytovatele zdravotních služeb vést zdravotnickou dokumentaci a poskytovat Vám péči. Zpracování údajů v Registru Vám nezakládá žádný závazek, není způsobilé Vám způsobit újmu. Údaje z databáze nebudou využity k nabízení jakýchkoli produktů či služeb. S ohledem na skutečnost, že se jedná o dlouhodobý statistický sběr, nelze předem odhadnout, po jak dlouhou dobu budou zaznamenaná data archivována a zpracovávána v registru. Poté co pomine jejich význam pro výzkumné záměry budou data smazána. Data o vaší léčbě MU nikdy nepředá jiným osobám.

Svůj souhlas se zpracováním osobních údajů máte právo odvolat, bez jakékoliv dopadu na Vaši další léčbu. Odvolání souhlasu můžete učinit prostým písemným oznámením Vašemu poskytovateli, který jako jediný subjekt může identifikovat, pod jakým kódem se vyskytují údaje právě o Vaší léčbě. Poskytovatel využije svých přihlašovacích údajů a smaže údaje spojeny s Vaším kódem.

Máte rovněž právo na informace, jaké osobní údaje o Vás MU nebo poskytovatel zdravotních služeb uchovává a za jakým účelem a máte právo na opravu či smazání dat, které se týkají Vaší osoby. S velkou pravděpodobností však obdržíte informaci, že MU není schopna z velkého souboru anonymních či pseudonymních dat identifikovat údaje právě o Vaší léčbě.

Máte právo kdykoliv kontaktovat MU nebo svého poskytovatele zdravotních služeb. V případě dotazů ohledně zpracování dat pro výzkumné účely nebo v otázkách opatření, které MU provádí v zájmu ochrany vašich osobních údajů se prosím obracejte na kontaktní údaje uvedené na webových stránkách http://empire.registry.cz/. Údaje o Vaší léčbě nebudou předávány mimo hranice EU.

Prohlášení pacienta

Já, ……., narozen(a) dne …….,

dávám plný a vědomý informovaný souhlas, aby můj poskytovatel zdravotních služeb ……(název a sídlo)…… sbíral a zpracovával data týkajících se průběhu mé léčby při mém onemocnění na ….. Prohlašuji, že jsem četl(a) text na předchozích stranách tohoto dokumentu, že jsem mu porozuměl(a) a případné nejasnosti mi byly vysvětleny.

Svým podpisem dávám na vědomí, že souhlasím s tím, aby data o mé léčbě byla mým poskytovatelem zdravotních služeb anonymizovaná/pseudonymizována a následně předána **Masarykově univerzitě**, IČ: 00216224, kterou tímto opravňuji k tomu, aby moje data dále zpracovávala k výzkumným účelům popsaným výše.

Souhlasím s tím, aby byla data o mé léčbě použita k výzkumným účelům pro výzkum Idiopatické plicní fibrózy a souvisejících onemocnění. Jsem informován(a) o skutečnostech, že mám právo požadovat od správce přístup ke svým osobním údajům, jejich opravu nebo výmaz, popřípadě omezení zpracování, a vznést námitku proti zpracování, jakož i o existenci mého práva na přenositelnost údajů a práva být informován o případech porušení zabezpečení osobních údajů. Jsem si vědom, že můžu tento souhlas kdykoliv odvolat a také že mám právo podat stížnost u dozorového úřadu.

Jsem si vědom, že v případě dotazů na způsob vedení registru se mohu obrátit na svého poskytovatele zdravotních služeb nebo přímo na pracoviště Masarykovy univerzity na adrese: Institut biostatistiky a analýz Lékařské fakulty MU, Kamenice 126/3, 625 00 Brno, Tel.: (+420) 549 49 4352.

V ……. Dne ……..

Podpis: ……

Jméno …… a podpis …….. zákonného zástupce.

Po tomto seznámení si nejsem vědom(a) žádných důvodů, které by mému souhlasu s registrací dat bránily a dobrovolně souhlasím s registrací klinických dat v registru Idiopatické plicní fibrózy České pneumologické a ftizeologické společnosti ČLS JEP.

_____ _____

Podpis pacienta Datum

S pacientem jsem s pomocí tohoto dokumentu vše prodiskutoval(a). Jsem přesvědčen(a), že jsem pacienta plně informoval(a) o podstatě projektu, jak je vyžadováno platnými etickými a legislativními normami a předám pacientovi jedno vyhotovení podepsaného a datovaného informovaného souhlasu.

_____ _____

Ošetřující lékař - jméno Datum