

9TH STEERING COMMITTEE MEETING IN GENEVA

MEETING MINUTES

Date Place: 1 April 2019, 18:15 – 20:15, Geneva, Warwick Hotel, Rue de Lausanne 14, Switzerland

Participants:

| | |
|------------------------|--------------------------|
| Martina Vašáková | Dragana Jovanovic |
| Veronika Müller | Katarzyna Lewandowska |
| Nesrin Mogulkoc | Biserka Jovkovska Kjaeva |
| Jasna Tekavec-Trkanjec | Karel Hejduk |
| Natalia Stoeva | Ondřej Májek |
| Michael Studnicka | Jakub Gregor |
| Martina Šterclová | |

This meeting minutes accompany the official presentation of the 9th SC meeting and summarise discussion from the 9th SC meeting.

Current status

- **Project team changes** – Jana Gregorová (project manager), Jakub Gregor (website, quality control), Karel Hejduk (senior PM), Ondřej Májek (senior data analyst), Lucie Martykánová (economics, administration)
- **3 new centres** – Serbia, Israel, Austria
- **1 terminated cooperation** – Croatia
- **9 centres from 5 countries are interested in participation** – Poland, Hungary, Romania, Latvia, Turkey
- **Contracts with centres** – 23 signed contracts, 28 contracts in progress
- **2,794 valid patients** by countries in the EMPIRE registry, 62 excluded patients from analyses due to unknown date of diagnosis or admission visit or changed diagnose
- **Support of registry** - Starting from 2019, there should be new contracts with **BI and Roche**, both will be supporting EMPIRE Registry. Legal department of Masaryk University (MU) negotiate contract (in cooperation with prof. Vašáková, BI and Roche)

News in the registry

- **Revised informed consents** – translated into local languages and available on the project website
- **Validation excel tables** – sent to physicians in centres (missing, incorrect, unknown, not logical data etc.) in order to ensure valid and complete data for patient records
- **De-identification of patients** – full dates of birth and initials of all patients in the database have been replaced by month and year of birth of the patients. It is possible to input the whole date of birth into the database (day/month/year); however, 10 minutes after that the system will

automatically change the day from the date into number 01 (meaning 1st day of the month). Information on month and year (01/month/year) stay as they are in all patients.

Voting and proposal of future analyses

- **Voting since previous meeting** - SC members voted by emails – answer: agree/disagree
- It was emphasised that **authors and investigators should primarily focus on completion of current analyses and publications** that are pending or under progress: “Bleeding” (V. Müller), “Comorbidities” (D. Jovanovic), “Prognostic factors” (T. Tran, S. Suissa), “Crepitus” (M. Studnicka)
- **Removal of stopping rules in the Czech Republic** – Data from registry will be used for negotiation with Czech regulatory authority; the analyses will be used for publication – the primary author will be Michael Studnicka
- **Genetics**, prof. Jovanovic – possible data collection in excel sheets and connection to the registry, possibly collaboration with prof. David Schwarz; we can process comparison for Turkey and Czech cohorts
- **ANCA** - data are not collected in registry, it is possible to collect in excel sheets and connection to the registry for analyses
- Further topics were discussed and may be suggested for analysis: TKI better response (V. Müller), IPF and lung cancer (N. Mogulkoc), risk assessment for mortality in IPF patients (N. Mogulkoc), Crepitus (Prof. Studnicka – pending), PPI (S. Suissa / T. Tran), differences between countries (V. Müller), metformin comedication (D. Jovanovic), Correlation of response to antifibrotic treatment with adverse events to antifibrotic drugs in IPF patients (D. Jovanovic), drug safety phenotypes, emphysema

Analyses and publications

- **Effect of pirfenidone on lung function progression and survival: 5-yr experience from a real-life IPF cohort from the Czech EMPIRE registry**, Dr. Žurková et al., published in Respiratory Research
- **Long-term effects and adverse events of nintedanib therapy in IPF Patients with functionally advanced disease**: Dr. Barczy et al. (Hungary), accepted for publication in Advances in Therapy
- **Prognostic factors in idiopathic pulmonary fibrosis: The European MultiPartner IPF Registry (EMPIRE) from Central and Eastern Europe**, Tanja Tran, rejected in the American Journal of Respiratory and Critical Care Medicine, will be submitted in another journal (SC members can propose the journal)
- **Comorbidity in IPF patients from EMPIRE registry (European Multipartner IPF registry)**, Dragana Jovanovic, prepared for submission
- **Bleeding risk in Central European IPF patients treated with different anticoagulants**, Prof. Veronika Müller, reanalysed for increase in the number of patients
- **Genetic polymorphisms in Czech patients**, Dr. Doubková, Dr. Žurková, doc. Kriegrová, in preparation
- **Long-term overall survival and progression-free survival in idiopathic pulmonary fibrosis treated by pirfenidone or nintedanib or their switch. Real world data from the EMPIRE**

registry, Prof. Martina Vašáková, submitted for ERS, and to be written as a fulltext paper by Prof. Yochai Adir

- **Differences between ANCA positive and negative lung fibrosis cases without vasculitis** (Turkish patients only), Prof. Nesrin Mogulkoc, submitted for ERS
- **Crepitus** – to be completed by Prof. Studnicka by the end of 2019
- **It is very important to publish outputs, particularly in impact factor journals, for justification of the registry**

HRCT subproject

- Protocol and budget currently reviewed by sponsors.
- PACS repository will be established by IBA on Masaryk University's servers.
- IBA will provide all investigators with a detailed user guide on the PACS system – how to send digital images from local system, how to handle images saved on a CD etc.
- It is necessary to complete the system establishment and images transfer and analysis by the end of 2019.
- The subproject will be registered at clinicaltrials.gov (IBA).
- IBA will apply for a local Ethical Committee approval.
- A specific informed consent will have to be prepared and signed by patients for this purpose (IBA).

PDL-1 subproject

- The study protocol and budget are now being finalised by IBA in cooperation with Prof. Jovanovic, the study initiator.
- After finalisation the protocol and budget will be provided to SC members and sponsors for review (IBA, April 2019). Participating centres will then be approached with an offer to participate in the study, with a primary focus on the most active centres with the highest numbers of patients in the registry.
- The subproject will be registered at clinicaltrials.gov (IBA).
- IBA will apply for a local Ethical Committee approval.
- A specific informed consent will have to be prepared and signed by patients for this purpose (IBA).

eCRF changes

- **Categorization of the HRCT appearances** – prof. Mogulkoc suggest updated four diagnostic categories currently recommended by ATS/ERS: 1) usual interstitial pneumonia (UIP) pattern, 2) probable UIP pattern, 3) indeterminate pattern, and 4) alternative diagnosis.
- **SC members agreed for a change in eCRF** in the HRCT categorisation (new code list). The SC members were aware of the fact that new patients/records would be incompatible in this parameter with the patients that have been registered to date.

Statistical comment

- Loss of observations in time is a critical issue. Namely, it is a problem in the analysis of time to event since IPF diagnosis, where only 1657 of 2794 potentially available patients have their valid baseline FVC value and the loss gets more substantial in time. It is lesser problem in analysis of time to event since enrolment. This should be taken into account when specifying IIS.
- Importance of accounting for left truncation when performing survival analysis when time origin (diagnosis, start of IPF treatment) is before baseline visit was explained. The analysis accounting for left truncation should be preferred.

Discussion

- Suggestion to **inform the principal investigator in centres** about paying out the finance to hospital, approved
- Mentioned **problem with validation of HRCT score** – IBA will check it
- Mentioned **problem with calculation % FVC/TLCO** – IBA will check it
- **recording of grading HRCT** – facultative for pulmonologist (important trained in this matter)
- **Promotion and publicity** – press conference (not important), Patients with IPF summit in 4/2020

10th Steering Committee meeting will be held in Madrid during ERS meeting, September 2019.

Drafted by: Karel Hejduk, Jakub Gregor

Approved by: Martina Vašáková