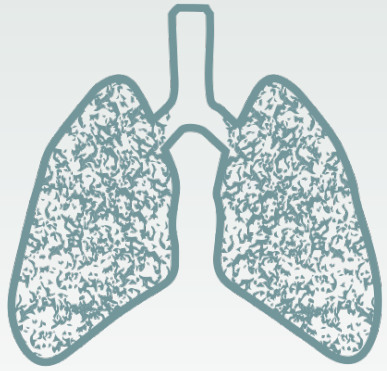

European Multipartner IPF Registry
10th SC meeting

Martina Vašáková[1], Jakub Gregor[2]

[1] Thomayer Hospital, Prague, Czech Republic;

[2] Faculty of Medicine, Masaryk University

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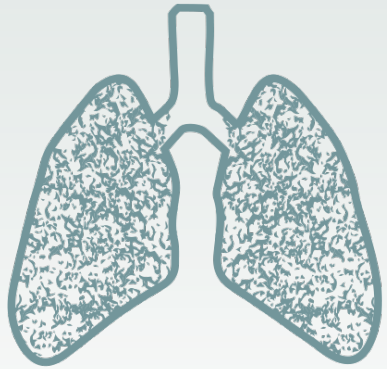

EMPIRE
(IPF)

Current state of the registry

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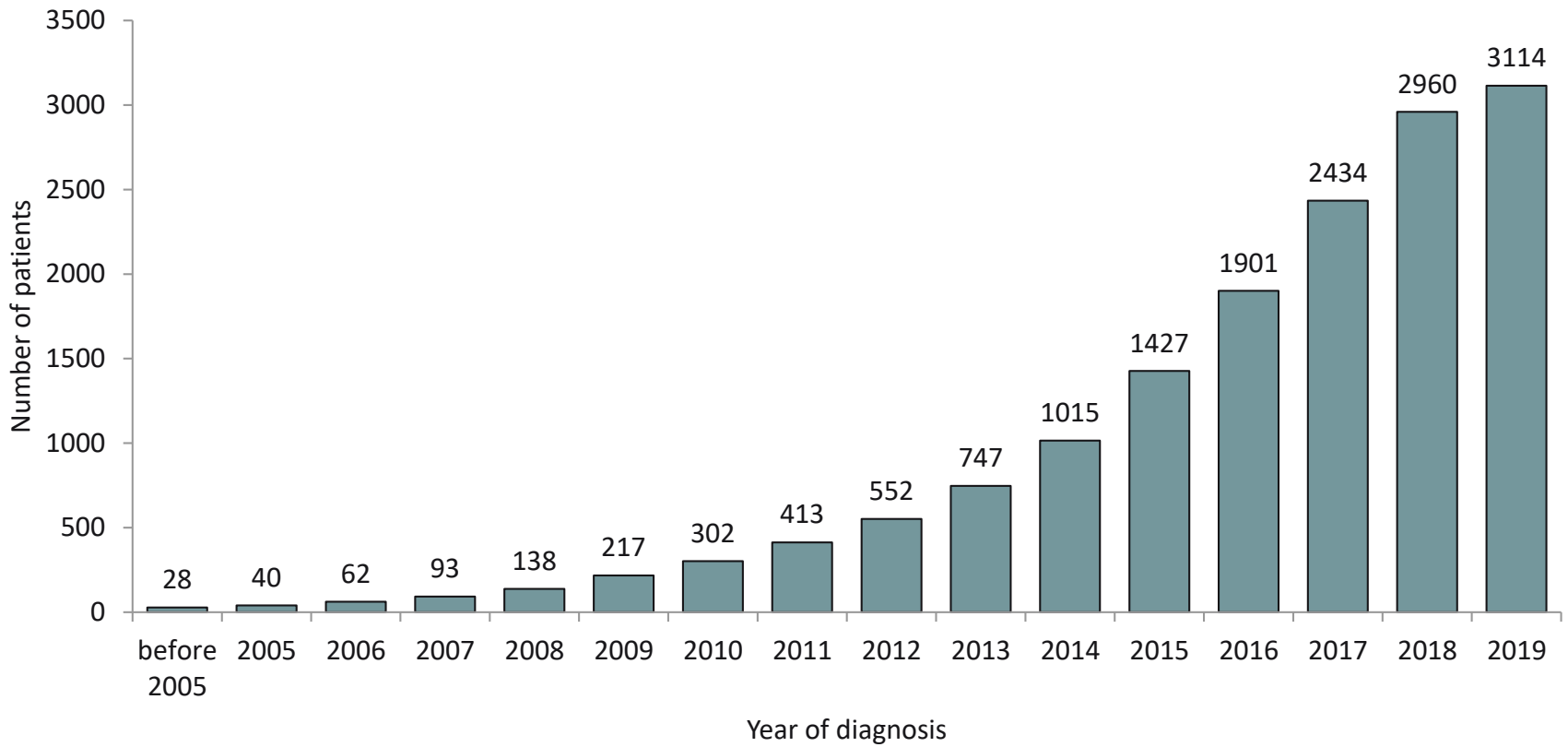
Number of newly diagnosed patients

n = 3,114

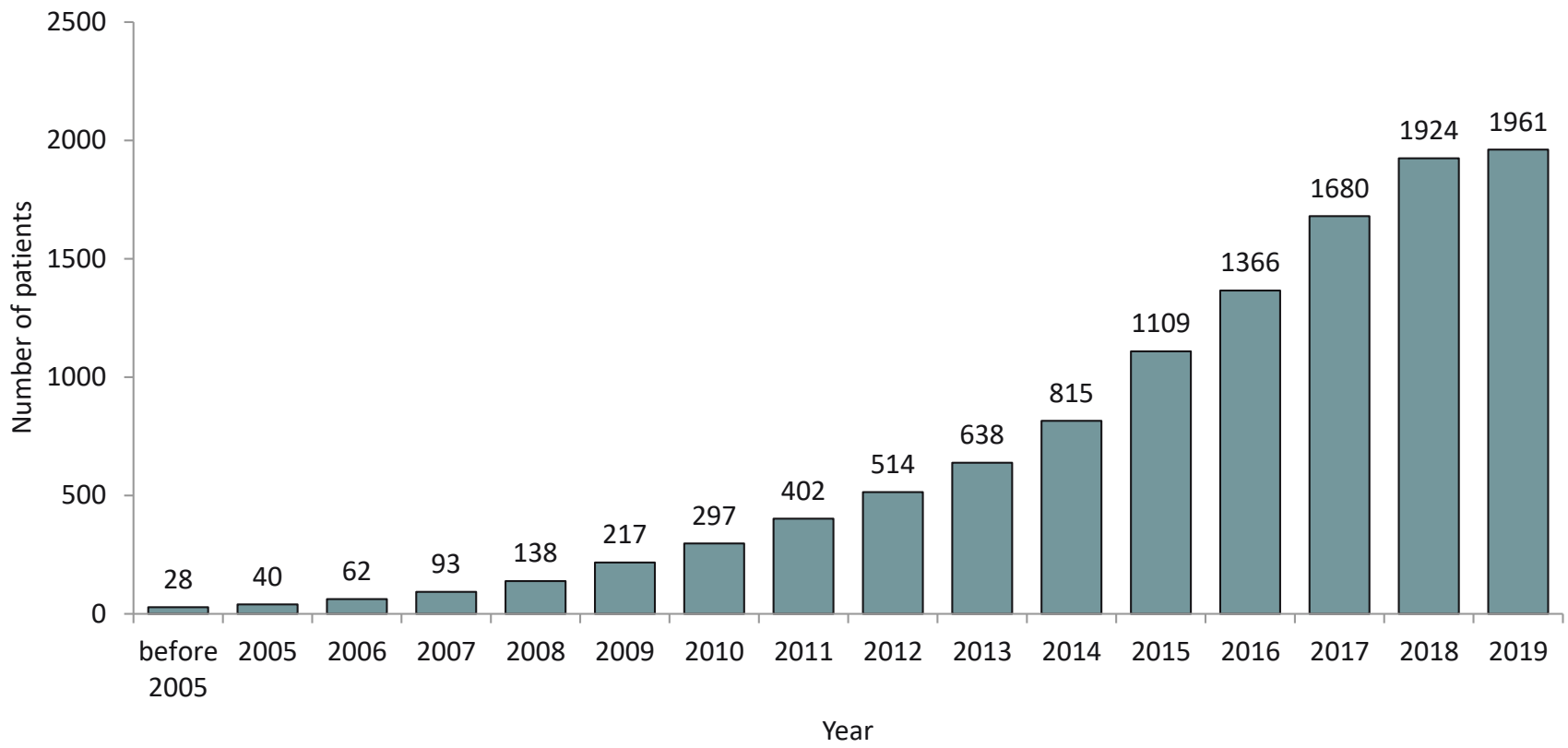


EMPIRE (IPF)

Number of monitored patients

n = 3,114

Year	Number of terminated follow-ups (with known date)
2010	5
2011	6
2012	27
2013	71
2014	91
2015	118
2016	217
2017	219
2018	282
2019	117
Total	1153



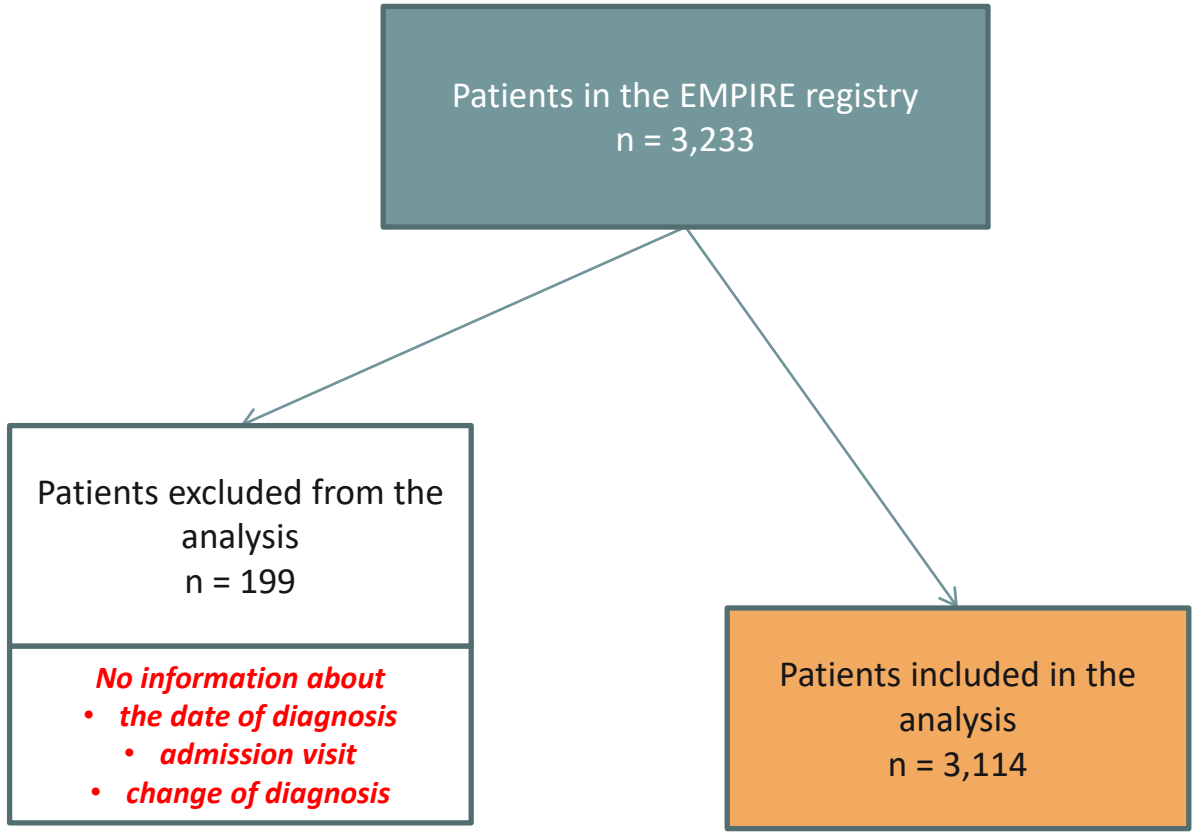
The number of patients in the EMPIRE registry monitored in a given year is reduced by the number of patients with terminated follow-up due to death (n = 765), lung transplantation (n = 51), patients lost from follow-up (n = 300), other (n = 37).
The date of death is unknown in 16 patients.

EMPIRE (IPF)

Number of valid patients by countries in the EMPIRE registry

n = 3,114

	Number of patients
Czech Republic	1020 (32.8%)
Turkey	588 (18.9%)
Poland	523 (16.8%)
Hungary	259 (8.3%)
Slovakia	205 (6.6%)
Israel	190 (6.1%)
Serbia	132 (4.2%)
Croatia	90 (2.9%)
Austria	86 (2.8%)
Bulgaria	17 (0.5%)



EMPIRE (IPF)

Representation of countries in the EMPIRE registry

11 countries, 50 centres

- Austria (2 centres)
- Bulgaria (1 centre)
- Croatia (2 centres)
- Czech Republic (16 centres) (1 terminated cooperation)
- Hungary (6 centres)
- Israel (2centres)
- North Macedonia (1 centre)
- Poland (9 centres)
- Serbia (4 centres)
- Slovakia (6 centres)
- Turkey (1 centre)

EMPIRE (IPF)

New countries/centres interested in participation

Country	Comment
Poland	1 new centre (Lublin) contacted in early 2019 (EC approval, contract sent), no response to date
Romania	Communication with Irina Strambu and Radu Crisan-Dabija
Latvia	Latvia would like to join EMPIRE (core information, documents sent to Alvils Krams), no response to date
Slovakia	1 new centre (Banska Bystrica) interested in participation

EMPIRE (IPF)

Contracts with centres

- **From April 2018 only contracts with the centres/hospitals are possible.**
- According to the new regulations that the Masaryk University has implemented and anticorruption law of the Czech Republic it is no longer possible to make direct agreements with data managers (investigators).
- Contract templates have been sent to all centres; the centres are obliged to pay the remuneration to the data managers.
- Please try to remind it to the centres in your country. If the contracts are not signed, the registry will not work and we will not be able to send payments.

EMPIRE (IPF)

Overview of contracts

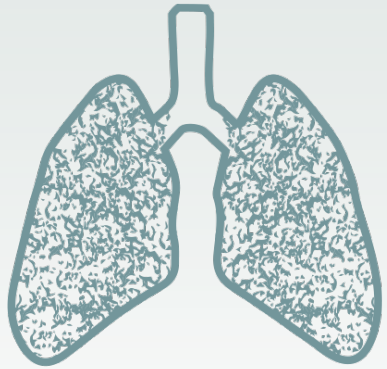
Country	No. of centres with signed contract	No. of centres without signed contract
Czech Republic	12	4
Hungary	2	4
Poland	4	5
Slovakia	3	3
Serbia	3	1
Turkey	0	1
Croatia	1	1
Israel	1	1
Bulgaria	1	0
Austria	2	0
Macedonia	1	0
Total	30	20

EMPIRE (IPF)

News in the contracts

- All current contracts have been effective by 31/12/2019.
- It will be necessary to sign an amendment (for centres that already signed the contract) to be effective by September 2022.
- The centres without contract will obtain a new contract to be effective by September 2022.

EMPIRE (IPF)



EMPIRE
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News in the registry

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Financial support

- After a meeting in January 2019, **Boehringer Ingelheim RCV and Roche Global agreed on supporting the EMPIRE Registry in the years 2019–2022**; the contracts should be concluded in September 2019.

- Since December 2017, an active contract with **Roche CZ** has been effective, which has supported an IIS study (financial support of the Czech part of the registry) led by Prof. Vašáková till the end of 2020. **This contract will be terminated by the new contract with Roche Global.**

- In cooperation with the Roche Global an IIS study *Assessing pirfenidone effectiveness in possible UIP and possible/probable IPF patients and characterizing natural history of IPF progression* has been prepared in order to support the registry.
  The contract/protocol/SAP was finalised in August 2019
  Data analysis underway

EMPIRE (IPF)

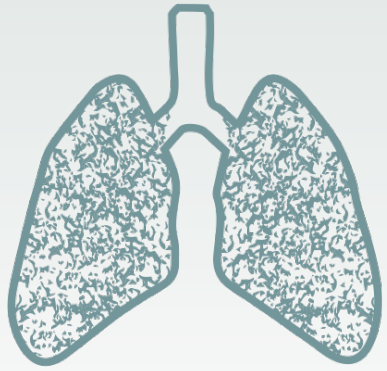
Quality of life of IPF patients in the registry

- A quality of life questionnaire (EQ-5D-3L) has been implemented as a part of the EMPIRE eCRF. A license for use of the questionnaire has been prolonged to 2021.
- Over 10,000 records = questionnaires have been collected in 2015–2018.

DISCUSSION/VOTING:

Is anyone willing to be a lead author of an article focused on the QoL?

EMPIRE (IPF)



Overview of SC members' votes since previous meeting

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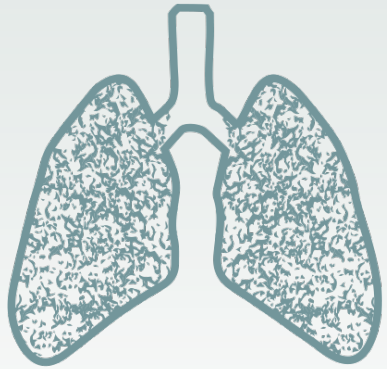
4 analyses/IIS proposed at 9th SC meeting in Geneva in April 2019

- **SC members approved processing of all four analyses**
  - Metformin – no objections
  - Cancer in IPF patients – no objections
  - Antifibrotics AEs – no objections
  - Risk assessment – notes on lack of some suggested parameters in the registry and partial duplication with the paper by Tanja Tran and Samy Suissa

EMPIRE (IPF)



Outcomes & publications

Published articles (IF journals)

2019

- Barczi E, Starobinski L, Kolonics-Farkas A, Eszes N, Bohacs A, Vašáková M, et al. Long-term effects and adverse events of nintedanib therapy in idiopathic pulmonary fibrosis patients with functionally advanced disease. Advances in Therapy 2019.
  IF = 3.085
- Žurková M, Eva Kriegová E, Kolek V, Lošťáková V, Šterclová M, Bartoš M, et al. Effect of pirfenidone on lung function decline and survival: 5-yr experience from a re al-life IPF cohort from the Czech EMPIRE registry. Respiratory Research 2019; 20: 16.
  IF = 3.751
  Times cited: 3 (Web of Science)

2018

- Doubková M, Švancara J, Svoboda M, Šterclová M, Bartoš V, Plačková M, et al. EMPIRE Registry, Czech Part: Impact of demographics, pulmonary function and HRCT on survival and clinical course in idiopathic pulmonary fibrosis. Clinical Respiratory Journal 2018; 12(4): 1526–1535.
  IF = 2.211
  Times cited: 5 (Web of Science), 7 (Scopus)

Articles in preparation / submitted

- **Prognostic factors in idiopathic pulmonary fibrosis: The European MultiPartner IPF Registry (EMPIRE) from Central and Eastern Europe**
  Lead author: Tanja Tran
  Current status: resubmitted to Respiratory Research (August 2019)
- **Anticoagulant use and bleeding risk in Central European patients with idiopathic pulmonary fibrosis (IPF) treated with antifibrotic therapy: real-world data from EMPIRE**
  Lead author: Abigél M. Kolonics-Farkas
  Current status: finalised by MW
  Note: recalculated on a new patient cohort in June 2019
- **Comorbidity burden in patients with idiopathic pulmonary fibrosis: the EMPIRE registry study**
  Lead author: Dragana M. Jovanovic
  Current status: finalised by MW

EMPIRE (IPF)

Analyses – finalised

- **Genetics in IPF patients**
  Investigator: Michaela Doubkova (CZ)
- **Stopping rules**
  Investigator: Martina Vasakova(CZ)
- **Intercountry differences in IPF patients**
  Investigator: Veronika Müller (HU)
- **Long-term overall survival and progression-free survival in idiopathic pulmonary fibrosis treated by pirfenidon or nintedanib or their switch**
  Investigator: Martina Vasakova (CZ)
  Note: used for a poster presentation at ERS 2019 and (after extension) a future publication by Yochai Adir

EMPIRE (IPF)

Analyses – underway

- **Correlation of response to antifibrotic treatment with adverse events to antifibrotic drugs in IPF patients from the EMPIRE registry**
  Investigator: Dragana Jovanovic; first round of analysis done
- **Cancer incidence among IPF patients in EMPIRE registry**
  Investigator: Nesrin Mogulkoc ; first round of analysis done
- **The effect of metformin on clinically relevant outcomes in IPF patients in the EMPIRE registry**
  Investigator: Dragana Jovanovic ; first round of analysis done
- **Risk assessment of mortality for IPF patients in EMPIRE registry**
  Investigator: Nesrin Mogulkoc; to be processed

Analyses – underway

- **Assessing pirfenidone effectiveness in possible UIP and possible/probable IPF patients and characterizing natural history of IPF progression: investigator-initiated study (secondary data use)**
  Investigator: Martina Vasakova; analysis underway
- **Turkish patients treated by pirfenidone**
  Investigator: Nesrin Mogulkoc; first round of analysis done

EMPIRE (IPF)

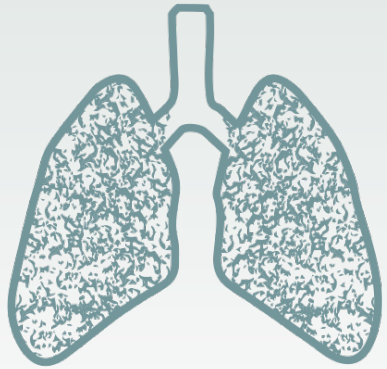
Publication outcomes – no reaction from co-authors

- SC members are included as co-authors of publications based on whole registry data
- A frequent problem – co-authors often do not respond to queries (both administrative and scientific) risen by lead/corresponding authors and/or medical writers
- **The process of publication preparation is significantly slowed down!**

VOTING:

If a co-author does not reply to a reminder by defined date, should this be taken that he/she is OK with all proposals?

EMPIRE (IPF)

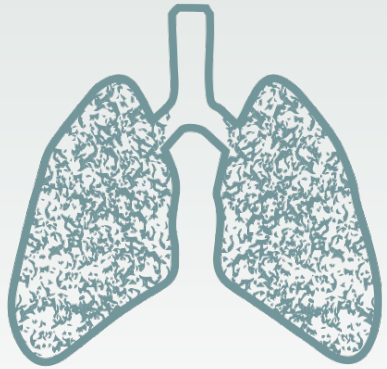


IIS proposals

IIS proposals

- Any SC member can ‘apply’ for writing a manuscript according to any IIS/analysis done – a rule **‘first come, first served’**
- **Planed IIS studies**
  Any new suggestions in addition to current analyses waiting for publication?
  (4 finalised and 6 underway)

EMPIRE (IPF)



EMPIRE
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Subprojects, IIS

HRCT Repository

Current status

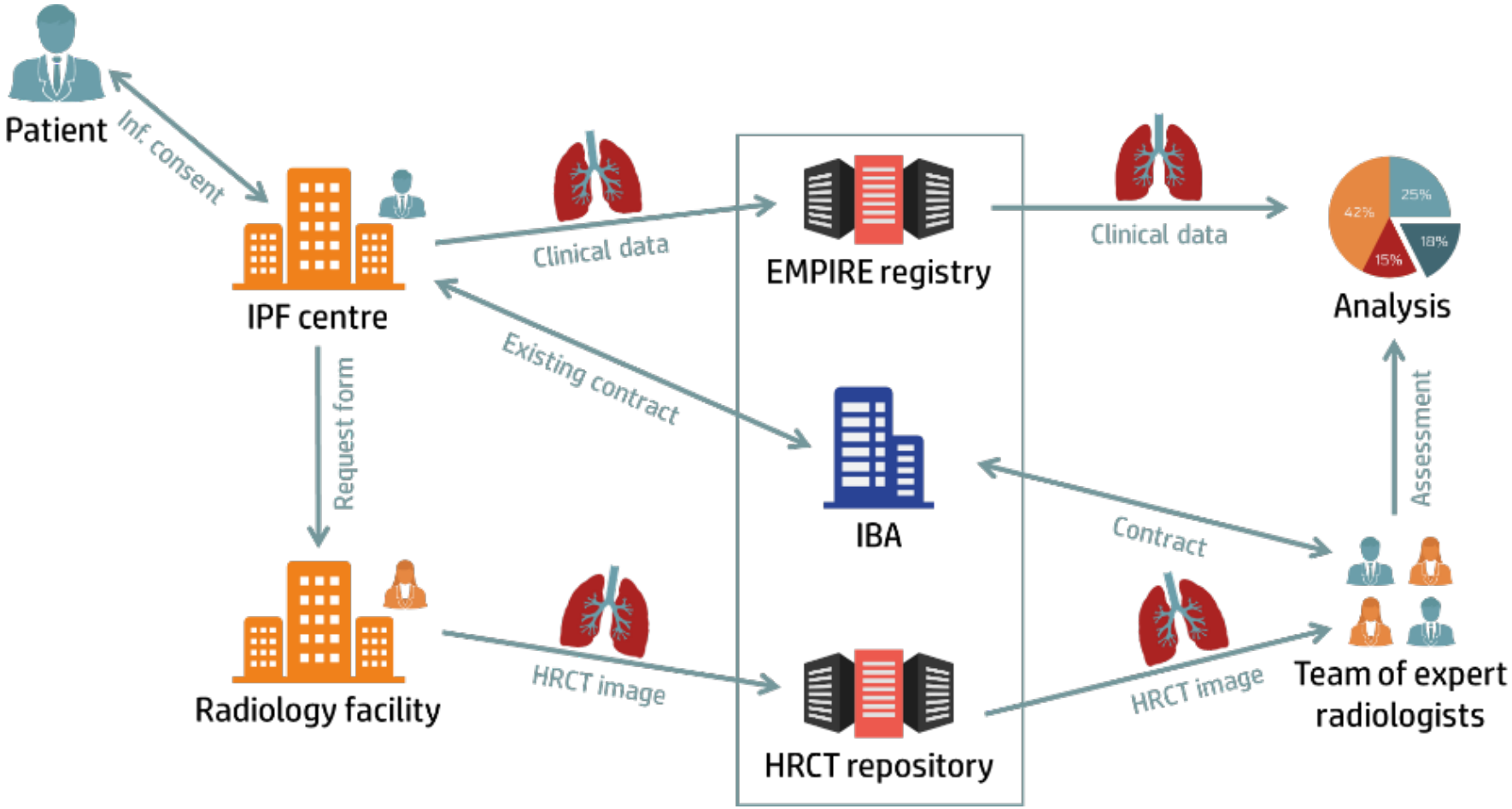
- Approved by the Ethics Committee
- Finalised protocol, informed consent, request form
- Drafts of user guides for EMPIRE centres, info graphics (to be reviewed)
- Investigators of EMPIRE addressed on 17/9 with information on the project and asked for notification on their (non-)participation
  (6 positive responses to date – Kragujevac, Gdansk, Linz, Izmir, Hradec Kralove, Nitra)

Project support

- Waiting for BI and Roche review and decision

EMPIRE (IPF)

HRCT Repository – data flow and processes



EMPIRE (IPF)

HRCT Repository – image upload

A user guide provided to centres on:

- Informed consent(s)
- Requests to radiologists to provide HRCT images for the study

Scenario 2

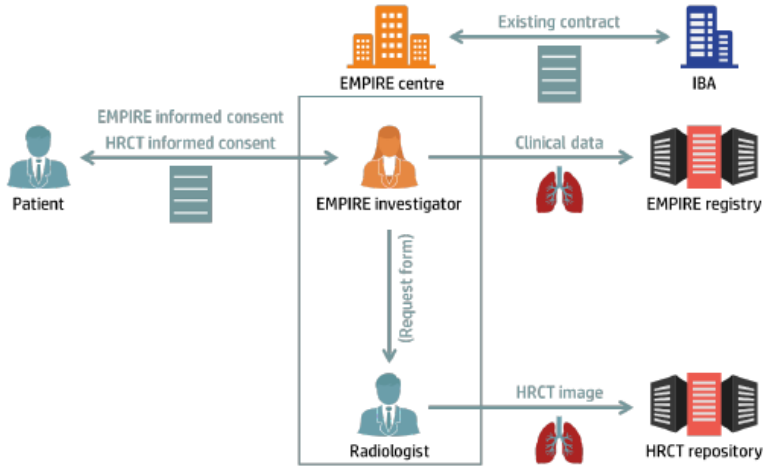
New patient, not included in the EMPIRE registry
HRCT images available in the EMPIRE centre (hospital)

EMPIRE informed consent (general)
- To be signed at the start of follow-up

HRCT informed consent
- To be signed together with the general informed consent

EMPIRE investigator
- Completes both informed consents
- Fills up and sends a request form to the radiology department in the hospital (if necessary)

Radiologist
- Finds HRCT images(s) of a respective patient in the repository (usually a local PACS system)
- Sends the HRCT image(s) to the EMPIRE-HRCT repository
- Communicates with the EMPIRE-HRCT repository administrator



HRCT Repository – important remarks

- A **standalone informed consent** (in addition to the general EMPIRE IC) is necessary
- Each patient must be **identified by his/her ID** in the EMPIRE registry in order to make possible subsequent de-identified connection of EMPIRE and HRCT data
- A patient with HRCT must have **valid records in the EMPIRE registry**, otherwise he/she cannot be included in the analysis
- Communication of EMPIRE centres with radiology facilities – on ad hoc basis
- HRCT images are considered to be part of health records, which are already entered into the EMPIRE registry by pulmonary centres, as stipulated in the contract with the Masaryk University

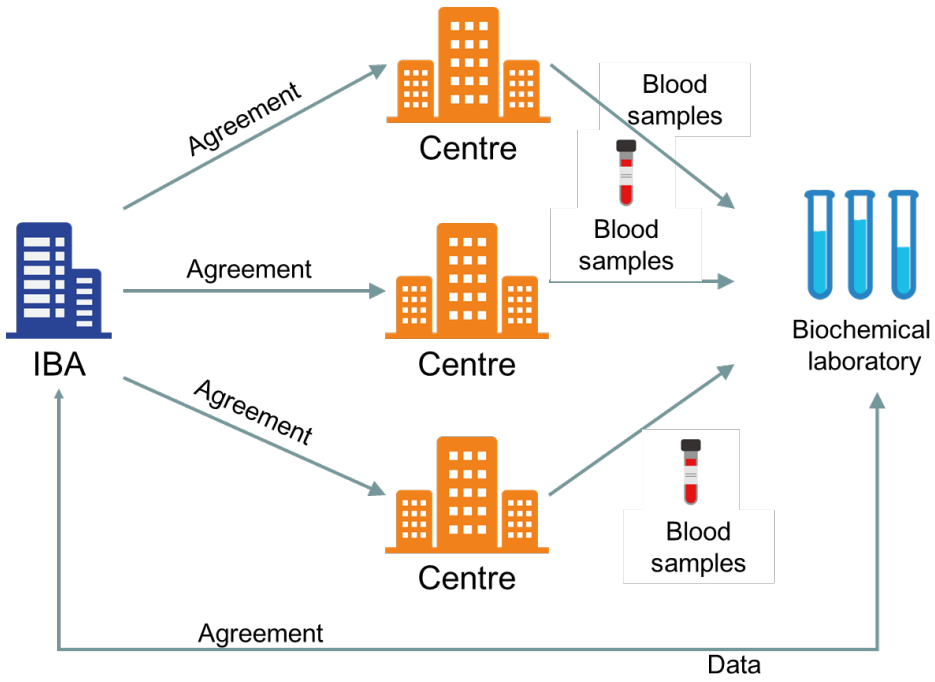
PD-L1 biomarkers

- Submitted for review to BI and Roche
- Team of Prof. Jovanovic will determine a soluble PD-L1 and serum amyloid A concentrations in blood plasma in IPF patients.
- Protocol, budget proposal and informed consent has been prepared.

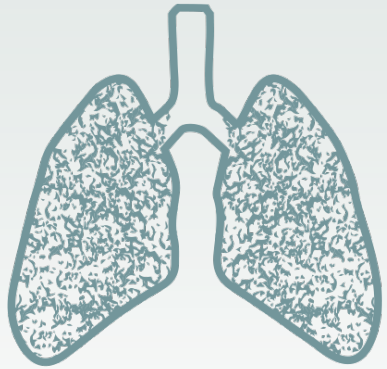
EMPIRE (IPF)

Determination of concentrations of soluble sPD-L1 in plasma and serum amyloid A (SAA) in patients with IPF

- The plasma samples from IPF patients will be transported to Belgrade for the PD-L1 and SAA analysis.
- The transport of plasma samples from participating centres to the Belgrade laboratory will be coordinated and ordered by IBA.
- The centres will be fully responsible for samples processing, storage, packing, and transmitting to the transport company.
- The transport of plasma samples will be provided by World Courier Czech Republic, Ltd.
  - The company provides all-inclusive transporting system that involves delivery of a packing system (polystyrene box, dry ice), solving every custom issues and other possible problems that are connected with the transport of hazard materials through borders.



EMPIRE (IPF)



EMPIRE
(IPF)

Registry rules, contracts, payments

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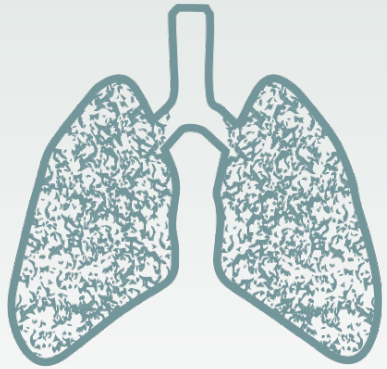
Publications submission

- Prior to any written, oral or audio-visual publication (manuscript, poster, abstract, presentation) of the results they have to be sent to BI and Roche.

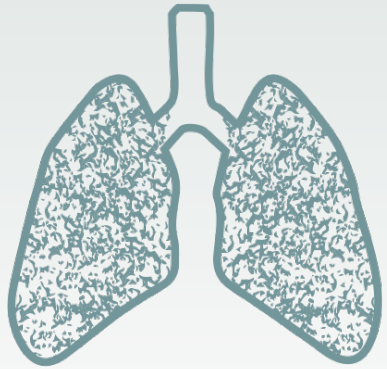
- To check whether all information presented/published are in line with SmPC and are compliant with their internal regulations. To protect a patentable invention or to avoid disclosure of Confidential Information, trade secrets or know-how. It is a fairly formal review of the manuscript/abstract.

Any other issues, proposals?

EMPIRE (IPF)



Time for discussion



Thank you for your time and attendance to the 10th SC meeting!

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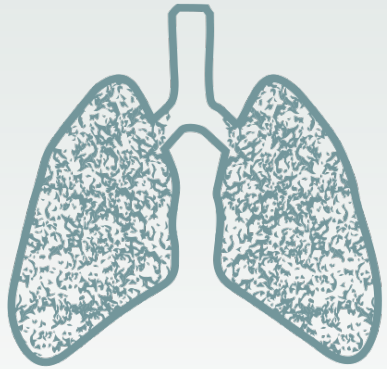

EMPIRE
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See you on the 11th SC meeting!

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