



EMPIRE
(IPF)

European Multipartner IPF Registry

13th SC meeting

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Agenda

- Current status of the EMPIRE registry
- Analyses underway
- Manuscripts in progress, publications
- Subprojects and their state (HRCT, PD-L1, new nintedanib IIS)
- Proposals for new analyses and IIS
- Extension of EMPIRE – other ILDs
- Continuation of EMPIRE after 06/2022



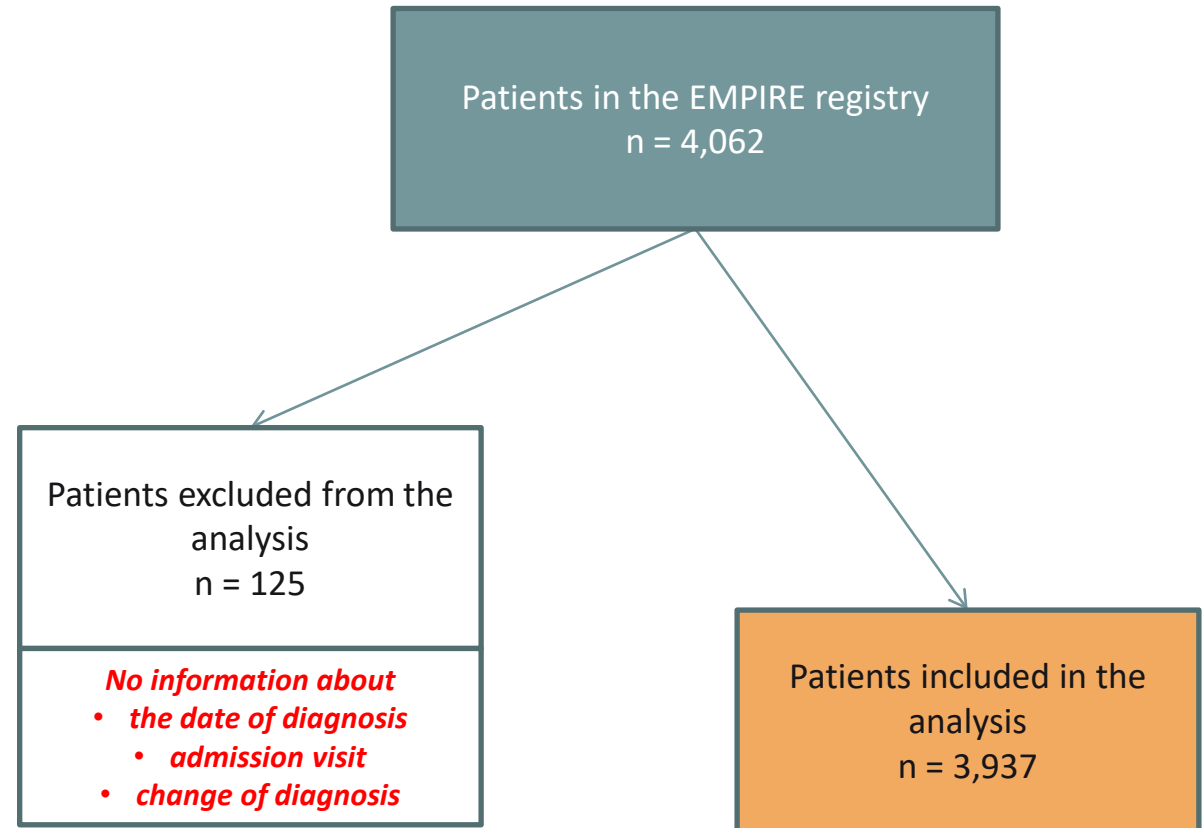


Current state of the registry

Number of patients by countries in the EMPIRE registry

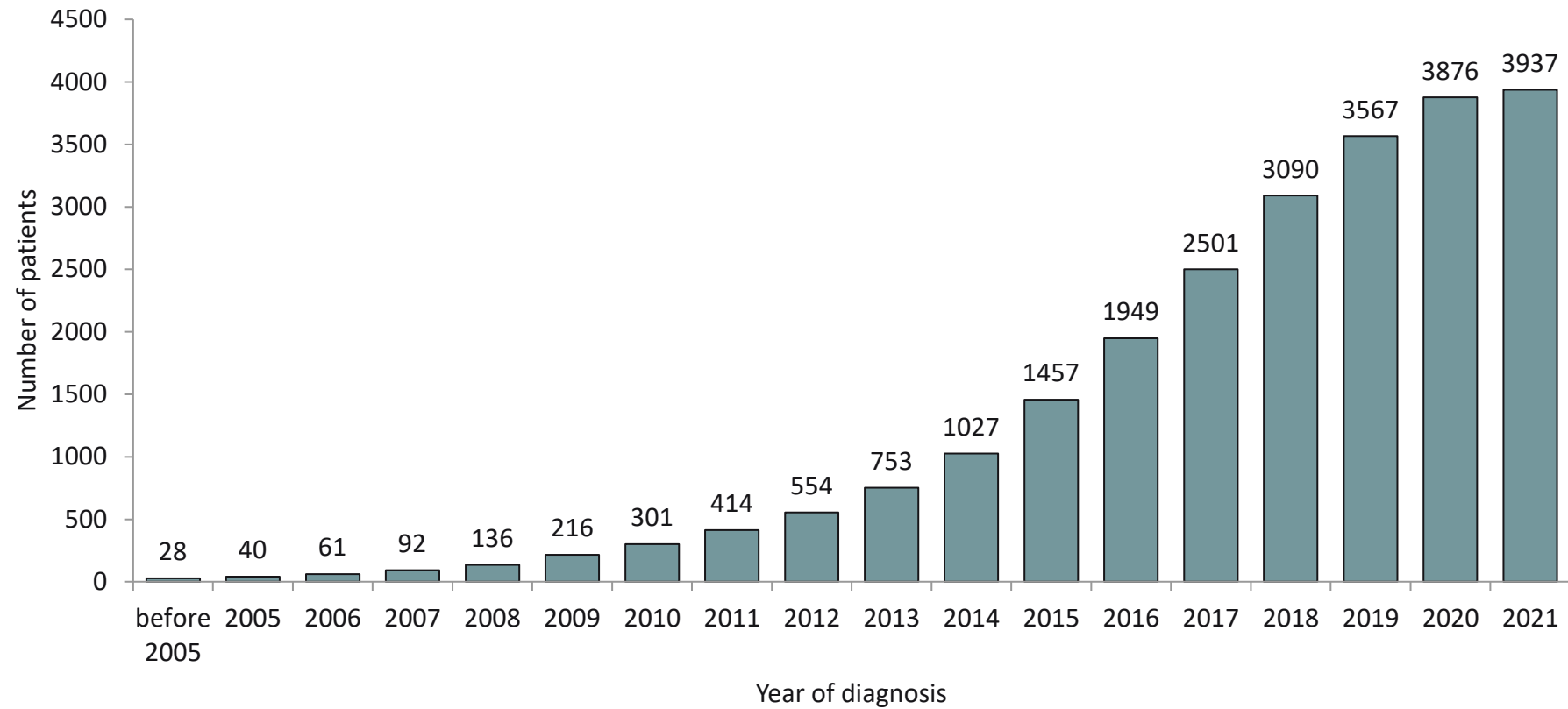
n = 3,937

	Number of patients
Czech Republic	1341 (34.1%)
Turkey	781 (19.8%)
Poland	609 (15.5%)
Hungary	291 (7.4%)
Israel	261 (6.6%)
Slovakia	234 (5.9%)
Serbia	155 (3.9%)
Austria	125 (3.2%)
Croatia	108 (2.7%)
Bulgaria	24 (0.6%)
Macedonia	8 (0.2%)



Number of newly diagnosed patients

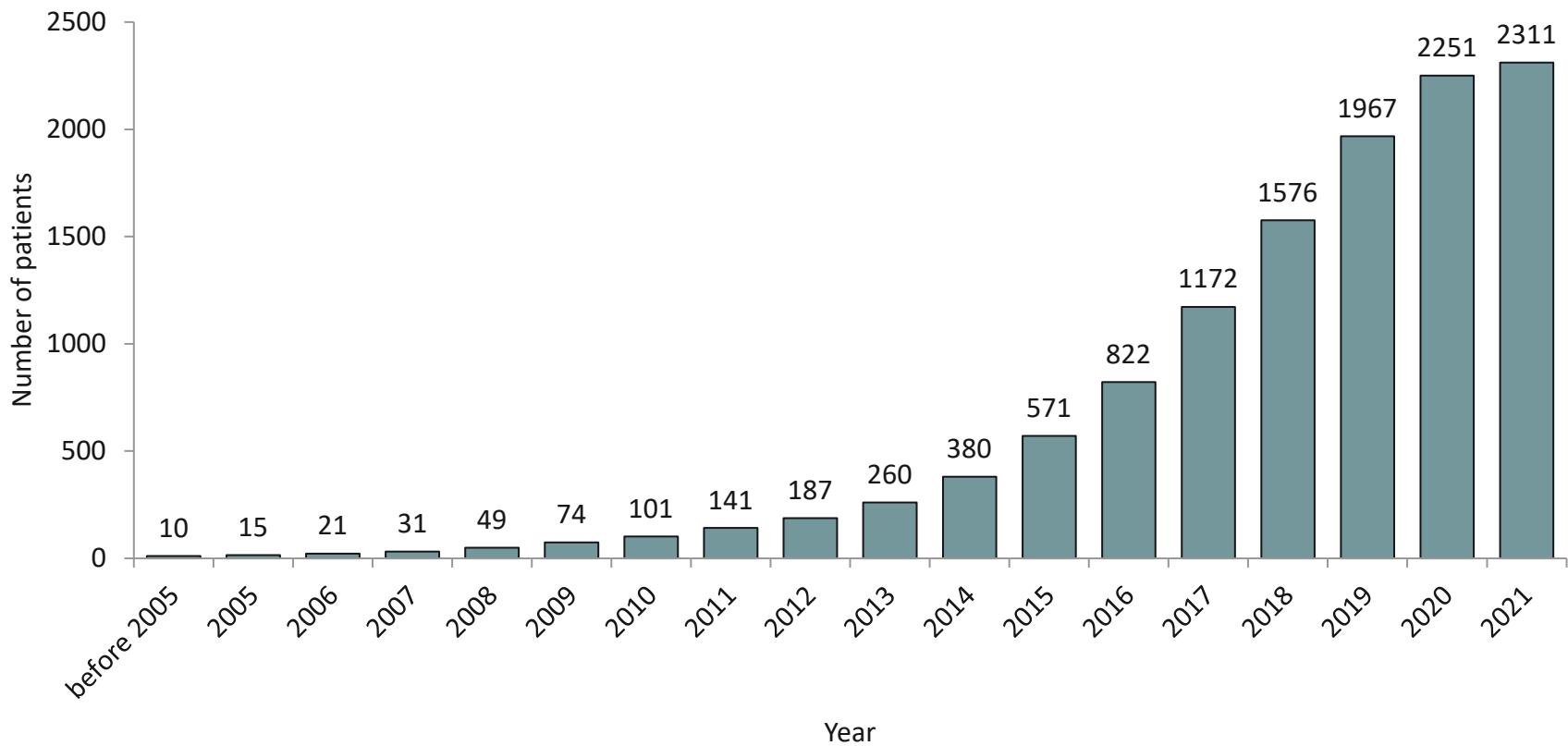
n = 3,937



Number of patients under follow-up

n = 3,937

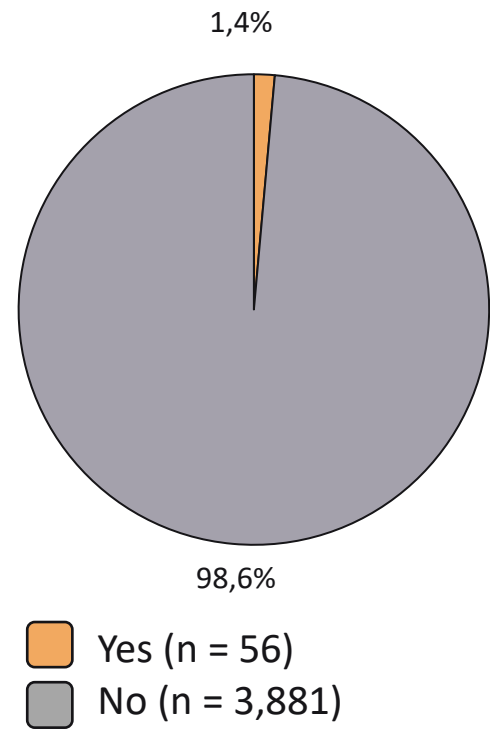
Year	Number of terminated follow-ups (with known date)
2010	5
2011	6
2012	27
2013	71
2014	91
2015	119
2016	218
2017	232
2018	304
2019	290
2020	213
2021	50
Total	1626



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 = 1,171), lung transplantation (n = 83), patients lost from follow-up (n = 337), other (n = 57).



Patients with COVID-19



	Number of patients	Age Mean (SD)	Deceased
Czech Republic	34 (60.7%)	71 (7)	4
Turkey	22 (39.3%)	70 (6)	5



Overview of contracts

Country	No. of centres with signed contract	No. of centres without signed contract	
Czech Republic	15	1	Hospital Znojmo
Hungary	2	4	Nat. Korányi TBC and Pulm. Institute, Budapest Debrecen University Clinical Centre, Debrecen Petz Aladár County Teaching Hospital, Győr University of Szeged, Szeged
Poland	4	5	Medical University of Silesia, Katowice Jagiellonian University, Kraków Medical University of Łódź, Łódź Poznan University of Medical Sciences, Poznań Medical University of Warsaw
Slovakia	4	3	University Hospital Bratislava L. Pasteur University Hospital Košice Specialised Hospital Zobor, Nitra
Serbia	2	2	Clinic for Lung Diseases Knes Selo, Niš Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica
Turkey	0	1	Ege University Medical School, Izmir
Croatia	1	1	Split University Hospital Center, Split
Israel	1	1	Carmel Medical Center, Haifa
Bulgaria	1	0	
Austria	2	0	
Macedonia	1	0	
Total	33	18	

New countries/centres interested in participation

Country	Comment
Romania	Communication with Irina Strambu and Radu Crisan-Dabija (no feedback to reminders)
Bulgaria	Military Medical Academy Sofia (contract pending), possible interest of other centres (information from BI)
Ukraine	Preliminary express of interest, information from BI

How we are doing – example Q1/2021

Clinical centre	Entry forms	F-up forms
Acibadem City clinic Tokuda hosp. Pulmonary dep.	1	1
České Budějovice - Plicní oddělení	0	8
Clinical Research Center Salzburg GmbH	5	33
EGE University - Department of Pulmonary Medicine	31	187
FN Brno - Plicní klinika	9	134
FN Motol - Pneumologická klinika	4	22
FN Olomouc - Plicní klinika	4	46
FN Ostrava - Klinika TRN	5	90
FN Plzeň - Klinika TRN	4	29
FNHK - Plicní klinika	6	87
Inst. of Tuberc. and Lung Dis. Warsaw - I Dep	4	45
Inst. of Tuberc. and Lung Dis. Warsaw - III Dep	1	5
Kepler University Hosp Linz – Dep of pulmonology	4	13
Kroměříž - Pneumologicko-alergolog. odd.	0	1
Levice - Ambulancia pneumológie a ftizeológie	1	5
Nemocnice Na Bulovce – Plicní klinika	3	6
Nový Jičín - Plicní odd.	0	21
Pécs University - Department of Pulmonology	2	16
Rabin Medical Center - Institute of Pulm. Medicine	4	4
Semmelweis University - Department of Pulmonology	1	22
Szpital Gdańsk. Uniw. Med. - Klin. Alerg. i Pneum.	8	88
Thomayerova nemocnice - Pneumologická klinika	9	170
	106	1033

Country	Entry forms	F-up forms
AT	9	46
BG	1	1
CZ	44	614
HU	3	38
PL	13	138
IL	4	4
SK	1	5
TR	31	187
Total	106	1033



SC voting since the last meeting

- **List of radiologists for the HRCT study**

Result: approved

- **IIS on nintedanib effectiveness in specific patient cohorts**

Result: approved

- **Joining the nintedanib multi-registry study**

Result: approved

Note: the study has been cancelled



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Analyses & publications

Published articles (IF journals)

2020

- Kolonics-Farkas A, Šterclová M, Mogulkoc N, Kus J, Hájková M, Müller V, Jovanovic D, Tekavec-Trkanjec J, Littnerová S, Hejduk K, Vašáková M. Anticoagulant use and bleeding risk in Central European patients with idiopathic pulmonary fibrosis (IPF) treated with antifibrotic therapy: real-world data from EMPIRE. Drug Safety 2020; 43(10): 971–980. Times cited: 2 (Web of Science), 2 (Scopus)
- Tran T, Šterclová M, Mogulkoc N, Lewandowska K, Müller V, Hájková M, Kramer MR, Jovanović D, Tekavec-Trkanjec J, Studnicka M, Stoeva N, Hejduk K, Dušek L, Suissa S, Vašáková M. The European MultiPartner IPF registry (EMPIRE): validating long-term prognostic factors in idiopathic pulmonary fibrosis. Respiratory Research 2020; 21: 11. Times cited: 4 (Web of Science), 3 (Scopus)

2019

- Barczy 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; 36(5): 1221–1232. Times cited: 4 (Web of Science), 6 (Scopus)
- 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 real-life IPF cohort from the Czech EMPIRE registry. Respiratory Research 2019; 20: 16. Times cited: 34 (Web of Science), 29 (Scopus)

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. The Clinical Respiratory Journal 2018; 12(4): 1526–1535. Times cited: 17 (Web of Science), 20 (Scopus)



Articles in preparation

- **Comorbidity burden in patients with idiopathic pulmonary fibrosis: the EMPIRE registry study**

Lead author: Dragana M. Jovanović

Current status: to be finalised

- **Genetics in Czech IPF patients**

Lead author: Martina Doubková

Current status: submitted in Therapeutic Advances in Respiratory Disease

- **Outcomes in patients with IPF in the EMPIRE registry treated with pirfenidone or nintedanib: impact of switching to a second antifibrotic therapy after discontinuation of the first antifibrotic**

Lead author: Yochai Adir

Current status: third draft circulating



Articles in preparation

- **Intercountry differences in IPF patients**

Lead author: Abigél M. Kolonics-Farkas

Current status: paper in preparation

- **Correlation of response to antifibrotic treatment with adverse events to antifibrotic drugs in IPF patients from the EMPIRE registry**

Dragana M. Jovanović

Current status: paper in preparation

- **Short- and long-term outcome of pirfenidone treatment in definite, probable and possible idiopathic pulmonary fibrosis**

Lead author: Martina Vašáková

Current status: under review in ERJ



Analyses – to be initiated

- Analyses previously agreed by the SC, but without specification to date
- **Crepitus**
Investigator: Michael Studnicka
- **Quality of life**
Investigator: Katarzyna Lewandowska
- **Genetics in Czech and Turkish cohorts**
Investigator: Nesrin Mogulkoc
- **Risk assessment**
Investigator: Nesrin Mogulkoc



Analyses – to be proposed and approved

- Analyses to be approved by SC
- **Extension of the pirfenidone radiological study (SDU)**

Investigator: Michael Studnicka





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Subprojects, IIS

HRCT Repository

Current status of financial support

- Direct support from Roche (half of costs) – contract signed in February 2021
- The grant agreement enables launching the repository

Repository operation

- Launch in May/June 2021
- Piloting phase by September 2021 – Czech centres



HRCT Repository

	Alive patients		Deceased patients	
Country	No.	%	No.	%
Czechia	854	36.0%	403	39.2%
Turkey	378	15.9%	346	33.7%
Poland	439	18.5%	78	7.6%
Serbia	79	3.3%	51	5.0%
Israel	188	7.9%	50	4.9%
Slovakia	152	6.4%	27	2.6%
Croatia	79	3.3%	26	2.5%
Hungary	121	5.1%	25	2.4%
Austria	70	2.9%	17	1.7%
Bulgaria	14	0.6%	4	0.4%
Total	2374	100.0%	1027	100.0%

No. of HRCTs images	No. of patients with HRCT images	No. of alive patients with HRCT images
1	1704	1223
2	757	500
3	427	297
4 and more	513	354
Total	3401	2374

HRCT Repository

Reading of images:

- Helmut Prosch (Austria)
- Eva Kočová (Czechia)
- Diana Manolescu (Romania)
- Pál Maurovich Horvát (Hungary)
- Recep Savas (Turkey)

❖ Emphysema

- Emphysema (yes/no)
 - Homogeneous
 - Heterogeneous

❖ Type of emphysema

- Centrilobular
- Panlobular
- Paraseptal

❖ Traction bronchiectasis

- Yes/No
- Number of lobes with bronchiectasis
min:1 max:5
- Maximum
 - In the central parts of the lung
 - In the periphery
 - Diffuse
- Predominantly
 - In the lower lobes
 - In the upper lobes
 - Diffuse

❖ Honeycombing

- Yes/No

❖ Ground glass opacities

- Yes/No
- Number of lobes *min:0 max:5*

❖ Mosaic attenuation

- Yes/No

❖ Craniocaudal gradient of interstitial changes

- Yes/No

❖ Lymphadenopathy

- Yes/No

❖ Nodules

- Yes/No

❖ Consolidation – Yes/No

❖ Reticulations - Yes/No

❖ Air trapping on expiratory scans (if available) – Yes/No

❖ Signs of pulmonary hypertension

- A1 (ascending aorta) (mm) (68239)
- A2 (descending aorta) (mm)
- A (average) (mm)
- PA (pulmonary artery) (mm) (68242)
- PA/A

UIP typical/ probable/indetermined for UIP/patterns highly consistent with non UIP



HRCT Repository

Cooperation with OSIC

- SC members agreed on cooperation with OSIC in the form of building a standalone EMPIRE-HRCT repository and subsequent provision of images to the OSIC database



PD-L1 biomarkers

- Support of the study from Roche (approved)
- Protocol, budget proposal and informed consent have been prepared
- Categorised as interventional (blood samples) – waiting for contract proposal from Roche
- Administrative issues – permission to import samples to Serbia from their MoH
- Alternative to perform the biochemical analysis elsewhere

Country/site	Number of samples	Collection – prospective	Collection – retrospective	Collection – routine	Collection – for the study
Czechia					
Hradec Kralove	50	yes	no	yes	no
Bulovka	20	yes	no	yes	no
Thomayer Hospital	40	yes	no	no	yes
Olomouc	20	yes	yes	yes	yes
Turkey					
Ege	400	yes	yes	yes	yes
Hungary					
Budapest	100	yes	no	yes	no
Croatia					
Dubrava	40	yes	no	no	yes



Nintedanib study

- Objective: analysis of short- and long-term clinical outcome of patients treated with nintedanib with different characteristics (FVC, HRCT, age, rapid/slow progression)
- IIS led by Martina Vašáková and supported by BI
- Current state: contract amendment and design in preparation

Characteristics of patients with rapid and slow progression

- Objective: clinical characteristics of patients that experience rapid and slow disease progression in its early phase
- IIS led by Martina Vašáková and supported by AstraZeneca
- Current state: to be specified





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EMPIRE in 2021, 2022...?

EMPIRE in the future

- Current contracts by 30 June 2022
- Support of BI and Roche from July 2022 onwards in negotiation
- Related points for further discussion (and timely conclusion):
 - Transfer of the EMPIRE database to a new platform (the current TrialDB platform will become obsolete)
 - Inclusion of other ILDs – create a different eCRF (new database), or extend the current one for IPF?
 - New Principal Investigator of the project?



Miscellaneous, discussion