ERS International Congress 2022: highlights from the Interstitial Lung Diseases Assembly

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Shareable abstract (@ERSpublications)
Early Career Members of @ers_ild summarise recent advances in translational and clinical research in idiopathic interstitial pneumonias, ILDs of known origin, sarcoidosis and rare ILDs presented at #ERSCongress 2022 https://bit.ly/3hcvqFf

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Abstract

This article contains a selection of scientific highlights in the field of interstitial lung diseases (ILDs) presented at the hybrid European Respiratory Society International Congress 2022. Early Career Members of Assembly 12 summarise recent advances in translational and clinical research in idiopathic interstitial pneumonias, ILDs of known origin, sarcoidosis and other granulomatous diseases, and rare ILDs. Many studies focused on evaluation of diagnostic and prognostic (bio)markers, and novel pharmacological and nonpharmacological treatment options for different ILDs. In addition, new insights in clinical, physiological and radiological features of various rare ILDs were presented.

Introduction

During the first-ever hybrid congress of the European Respiratory Society (ERS), numerous conference sessions focused on interstitial lung diseases (ILDs). Exciting scientific advances were presented during four oral presentation sessions and several poster presentation sessions. In the guideline, expert view, state-of-the-art and hot topic sessions, participants were updated on the new guidelines for idiopathic pulmonary fibrosis (IPF)/progressive pulmonary fibrosis, combined pulmonary fibrosis and emphysema, (cryo)biopsy in ILD, holistic patient management and pulmonary rehabilitation, patient journey in connective tissue disease (CTD)-associated ILD, and management of complicated sarcoidosis. The programme also included a Lungs on Fire session, in which complex ILD patient cases were interactively discussed. These sessions were livestreamed, and followed by clinicians and researchers from all over the world.

This article summarises scientific highlights presented in the oral presentation sessions for all groups of Assembly 12: group 12.01, "Idiopathic interstitial pneumonias" (IIPs); group 12.02, "ILDs/diffuse parenchymal lung diseases (DPLDs) of known origin"; group 12.03, "Sarcoidosis and other granulomatous ILDs/DPLDs"; and group 12.04, "Rare ILDs/DPLDs".

Idiopathic interstitial pneumonias

During the last decade, we have witnessed a scientific explosion in the field of IIPs. Nevertheless, there are still many unmet needs. These include identification of clinically applicable biomarkers, novel (non) pharmacological treatment options and interventions to improve health-related quality of life. At this ERS Congress, novel studies aiming to address these unmet needs were presented.

Several studies focused on identification and evaluation of potential new biomarkers. Analyses of two independent cohorts of patients with IPF validated the prognostic role of matrix metalloproteinase (MMP)-7. In particular, patients with an annual decline in forced vital capacity (FVC) ⩾10% had higher baseline MMP-7, whereas baseline MMP-7 >5.18 $\mu g \cdot L^{-1}$ was associated with greater probability for disease progression. These results suggest that biomarker-based enrichment strategies focused on MMP-7 levels may allow identification of patients with similar progression and/or enhance drug development in IPF [1]. Retrospective data from eight centres in six European countries showed that the *MUC5B* rs35705950 minor allele (T) was associated with older age and better survival in patients with IPF aged ⩾56 years at diagnosis [2]. With regards to theragnostic biomarkers, electronic nose (eNose) sensor technology yielded promising results. Before treatment initiation, eNose technology may already predict response to either antifibrotic or immunosuppressive treatment in patients with ILD. These results add to previous evidence for the diagnostic accuracy of eNose technology in ILD and imply great potential value in guiding treatment decisions in the future [3, 4]. Larger studies with long-term follow-up are greatly anticipated.

In addition, various studies evaluated the prognostic role of clinical parameters. Nocturnal hypoxaemia was shown to be associated with worse survival in patients with fibrotic ILD; therefore, further trials evaluating the role of nocturnal oxygen supplementation are needed [5]. A Belgian study in patients with IPF showed that a family history of a first-degree relative with ILD was significantly associated with FVC decline in a multivariate analysis. These data should be considered when informing patients about disease course [6]. The report that management of patients with ILD in specialised centres was associated with reduced mortality and reduced risk of 1-year all-cause hospitalisations compared to management in nonspecialised centres highlights the need for timely referral and closer cooperation among centres [7].

Data on pharmacological treatment for IIPs were also presented at the Congress. Preferential inhibition of phosphodiesterase (PDE)4B has emerged as a promising target in IPF [8]. A *post hoc* analysis of the BI 1015550 phase II study suggested it may have more pronounced effects on preventing FVC decline in patients with IPF if taken with nintedanib than with pirfenidone [9]. Of note, diarrhoea was the most frequently reported adverse event. The above data should be interpreted with caution due to the small sample size and the exploratory nature of this study. Phase III studies investigating the efficacy and safety of BI 1015550 in patients with IPF (FIBRONEER-IPF) and progressive pulmonary fibrosis (FIBRONEER-ILD) are ongoing (ClinicalTrials.gov identifiers NCT05321069 and NCT05321082).

The ongoing phase II, multicentre, open-label, single-arm, 36-week AIR trial aims to investigate the safety, efficacy and pharmacokinetics of the angiotensin II type 2 receptor (AT2R) agonist C19 in patients with IPF. The rationale of testing C19 in IPF is based on the following observations: 1) senescent or dysfunctional alveolar epithelial type II cells (AEC2) have a role in a failed healing process, 2) AT2R is exclusively expressed on AEC2 cells in the lung, 3) C19 is an AT2R agonist and 4) C19 stimulates alveolar progenitor cells to prevent pulmonary fibrosis development. Interim results suggested that C19 may improve lung function in individuals with IPF not previously treated with antifibrotic therapy. C19 was well tolerated with no treatment-related serious adverse events and no signals of gastrointestinal toxicity [10].

Importantly, results of the first randomised controlled trial (RCT) evaluating safety of nintedanib in children and adolescents with fibrosing ILD were presented. In the InPedILD trial, 39 children (mean age 12.6 years) were treated with nintedanib (n=26) or placebo (n=13). Adverse events were similar in both groups, with diarrhoea being the most common adverse event in the nintedanib group (38.5%). At week 24, FVC was stable in the nintedanib group (+0.3%) and showed a decline of 0.9% in the placebo group. These differences were not statistically significant but the study was not powered to assess change in FVC [11].

An interim analysis of a phase 2 trial showed promising results for the management of chronic cough, which exerts a dramatic impact on quality of life of patients with IPF. An extended-release (ER) oral form of the dual-acting κ-opioid receptor agonist/μ-opioid receptor antagonist, nalbuphine, was evaluated in IPF. Nalbuphine ER 27 mg once daily was titrated up to 162 mg twice daily at day 16. The compound had a favourable safety profile with a discontinuation rate of 16%, while no new safety concerns were raised. Nalbuphine ER demonstrated a highly significant and consistent reduction in chronic cough associated with IPF, but final study results should be awaited [12].

A few studies evaluated different aspects of pulmonary rehabilitation (PR). Two studies, one in IPF (n=235) and one in a broader group of ILDs (n=46), assessed the impact of pulmonary rehabilitation on anxiety and depression [13, 14]. PR significantly reduced anxiety and depression scores in patients with high scores at baseline. Samuel Santos *et al.* [14] reported a more pronounced beneficial effect of PR on anxiety than on depressive symptoms. A small pilot RCT (n=40) investigated the effects of a physical activity telecoaching programme in patients with ILD. After 3 months, steps per day, exercise capacity and muscle strength did not differ between the telecoaching and usual care group [15].

ILDs/DPLDs of known origin

About 20% of all ILDs are associated with underlying CTD, and major advances have been made in our understanding of CTD-ILD in recent years. Several important findings were presented, mainly in patients with systemic sclerosis (SSc)-associated ILD. Most studies focused on identifying predictors of disease progression and/or mortality.

Two *post hoc* analyses of the SENSCIS trial were presented. In patients with SSc-ILD, lower FVC or diffusing capacity of the lung for carbon monoxide (D_{LCO}) are associated with an increased risk of mortality, but it is unclear whether they are also associated with greater short-term decline in lung function. In the SENSCIS trial, nintedanib reduced the rate of decline in FVC over 52 weeks by 44% compared to placebo in SSc-ILD patients [16]. Wells *et al.* [17] assessed the efficacy of nintedanib in patient subgroups with differing lung function impairment at baseline. Patients who had worse baseline lung function had a greater rate of decline in FVC over 52 weeks. However, nintedanib slowed the decline in FVC irrespective of lung function impairment at baseline. Across the subgroups, fewer patients treated with nintedanib than with placebo met the threshold for worsening of FVC (defined as decrease in FVC ⩾3.3% predicted) and more patients met the threshold for improvement in FVC (increase in FVC ⩾3.0% predicted). Kreuter *et al.* [18] subgrouped patients from the SENSCIS trial by monocyte and neutrophil count. The rate of decline in FVC over 52 weeks was numerically greater in subjects with a monocyte count above than below the mean at baseline, but similar in subjects with a neutrophil count above or below the mean. However, a higher neutrophil count at baseline was associated with a greater risk of ILD progression or death. Nintedanib reduced the rate of decline in FVC irrespective of the monocyte or neutrophil count at baseline.

EUSTAR (European Scleroderma Trials and Research group) is a prospective observational cohort of patients with SSc. A persistent inflammatory phenotype was defined by a C-reactive protein (CRP) level ⩾5 $mg \cdot L^{-1}$ at ⩾80% of the visits. SSc-ILD patients with a persistent inflammatory phenotype had a shorter time from diagnosis, more severe ILD and were more frequently treated with immunosuppressants at baseline. This phenotype was associated with a more than five times higher risk of mortality independent of demographics, SSc subset, treatment and pulmonary function. Repetitive CRP measurements might facilitate therapeutic decisions and estimation of prognosis [19]. In the EUSTAR cohort, the mean FVC change in SSc-ILD patients over the first 12 months was −0.1%. This pattern of progression creates major challenges for clinical trial design and underscores the need for effective strategies to enrich clinical trials for patients with progressive SSc-ILD. However, it is unclear whether and to what extent enrichment strategies from clinical trials can be used in real-life patient cohorts. Hoffmann-Vold *et al.* [20] applied the inclusion criteria of major recent SSc-ILD trials (focuSSed, SENSCIS and SLS II) to the EUSTAR cohort. They found that none of the enrichment strategies showed a significant association with ILD progression. The authors concluded that use of these enrichment strategies will reduce feasibility for potential recruitment into clinical studies, without identifying patients at high risk of progression.

MicroRNAs (miRNAs) in plasma-derived exosomes may serve as noninvasive biomarker of lung involvement in SSc. In a study by Njock *et al.* [21], exosome was isolated from plasma of healthy controls, and SSc patients with and without ILD. 17 altered exosomal miRNAs associated with lung impairment were identified. Larger studies should be performed to validate the role of specific miRNAs as a biomarker in patients with SSc-ILD. Several novel autoantibodies are associated with different organ

manifestations in SSc. Stock *et al.* [22] found that autoantibodies to CD47 and KDM69 are associated with absence of ILD, whereas autoantibodies to TRIM21 (Ro-52) are associated with worse survival. If confirmed, these novel autoantibodies could aid in early and more precise phenotyping of SSc patients.

A number of studies focused on other CTDs. A phase II randomised trial (TRAIL1), which was terminated early due to coronavirus disease 2019 (COVID-19), investigated safety, tolerability and efficacy of pirfenidone in 123 patients with rheumatoid arthritis (RA)-associated ILD. This study did not meet the composite primary endpoint of a decline of ⩾10% in FVC during the 52-week study period. However, pirfenidone significantly slowed FVC decline compared to placebo (–66 *versus* −146 mL), with effects most pronounced in patients with a unusual interstitial pneumonia pattern on high-resolution computed tomography (HRCT) [23]. In the ongoing multi-centre prospective FIND-RA study, interim analyses have shown that older age, lower D_{LCO}, anti-cyclic citrullinated peptide antibody positivity and higher DAS28-CRP score are associated with ILD in patients with RA. The study, which is still ongoing, will also assess the association of lung involvement with *MUC5B* rs35705950 variant [24].

About one-third of non-IPF fibrotic ILD patients develop a progressive phenotype over time. To date, there are no validated biomarkers to predict progression in ILD. Serum levels of KL-6, a lung epithelial mucin, have been associated with disease severity in ILD, but its ability to predict progression pulmonary fibrosis remains to be established. In the VAMOS study, serum KL-6 levels at baseline did not differ based on ILD subtype but were higher in progressors than in non-progressors at 1 year. Five variables (age, gender, body mass index, serum KL-6 and FVC % predicted at baseline) were identified as predictors of disease progression at 1 year. A final score based on these parameters yielded a good sensitivity to predict disease progression at 1 year, superior to any individual predictor. The inclusion of serum KL-6 in a risk score may improve prediction of disease behaviour at 1 year regardless of the underlying ILD [25].

Patients with idiopathic inflammatory myopathy (IIM) can develop ILD during the course of the disease. However, it is still unclear which patients are at risk for lung involvement or progressive disease course despite treatment. Cocconcelli *et al.* [26] followed 253 IIM patients, 125 of whom developed ILD. IIM-ILD patients had lower creatine phosphokinase levels at diagnosis. Mechanic's hands, anti-Jo-1, anti-MDA5 and anti-Ro52 antibodies were independent predictors for the occurrence of ILD in patients with IIM. Almost one-fifth of the IIM-ILD patients developed a progressive phenotype, which was predominantly associated with anti-MDA5 antibodies, heliotrope rash, xerostomia and xerophthalmia.

Sarcoidosis and other granulomatous ILDs/DPLDs

The oral presentations about sarcoidosis focused on diagnosis, comorbidities, prognosis and treatment. The same session included two presentations about the pathogenesis and treatment of chronic hypersensitivity pneumonitis.

Two studies aimed to further elucidate diagnostic approaches in sarcoidosis. A large retrospective study (n=308) evaluated the diagnostic value of different endoscopic procedures. The researchers compared endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA), transbronchial biopsy (TBB) and cryobiopsy. They showed that confirmation of diagnosis was more common through EBUS-TBNA (69%) compared to TBB (59%) and cryobiopsy (60%), but only if the acquired material was of sufficient quality. This caveat should be considered carefully; indeed, it cannot be assumed these findings translate to those seen in daily practice, as sampling errors are not uncommon. The diagnostic yield improved to 93.8% when combining EBUS-TBNA and cryobiopsy, which was higher than EBUS-TBNA in combination with TBB [27]. Raniszewska *et al.* [28] looked at the lymph node aspirates in 29 patients, quantifying individual lymphocyte subpopulations. They reported a significantly higher percentage of $CD4^+$ T-cells, Th17 and $TregRO^+$ $CD95^+$ cells, without different levels in peripheral blood. The results suggested that an imbalance between Th17 and regulatory T-cells exists in patients with sarcoidosis.

To predict lung function decline, a retrospective study evaluated pulmonary function tests in 196 patients with fibrotic sarcoidosis. Four FVC trajectories were identified using statistical modelling. The group with the lowest FVC at inclusion (group 1, mean FVC 52% of predicted) showed a decline of 0.46%/year. The other groups remained relatively stable over time. Group 1 showed an increased risk of lung transplantation and hospital admission, possibly due to a higher risk for development of pulmonary hypertension compared to the other three groups [29].

Regarding prognostic tools in cardiac sarcoidosis, a retrospective analysis using speckle tracking echocardiography (STE) aimed to identify markers for major adverse cardiac events (MACE) and relapses.

Basal left ventricular global longitudinal strain was significantly lower in patients with MACE, whereas a reduction in left ventricular ejection fraction, tricuspid annular plane systolic excursion and global peak atrial longitudinal strain (PALS) were predictive of sarcoidosis relapse. PALS <28.5% was the strongest predictor of a sarcoidosis relapse [30]. These results indicate that STE might be used in clinical management of these patients in the future.

With regard to treatment for sarcoidosis, two Dutch studies addressed specific difficulties in treating sarcoidosis. A randomised controlled trial in patients with sarcoidosis-associated fatigue evaluated online mindfulness-based cognitive therapy (eMBCT) as treatment for fatigue, anxiety and depressive symptoms. Fatigue is one of the most commonly reported and burdensome symptoms in sarcoidosis, and is associated with anxiety and depressive symptoms. In this trial, patients with stable sarcoidosis who had no medication changes in the previous 3 months, were eligible for inclusion. The patients were randomised between eMBCT or standard care. Immediately after completion of eMBCT and 3 months later, patients reported significantly reduced anxiety and depression scores, measured with the hospital anxiety and depression scale. Furthermore, eMBCT improved the scores on Freiburg mindfulness inventory and general health domain of the King's Sarcoidosis Questionnaire; these effects sustained after 3 months. These findings show that eMBCT can be an effective treatment in an otherwise difficult to treat phenomenon in sarcoidosis [31]. A retrospective study evaluated effectiveness of hydroxychloroquine monotherapy in sarcoidosis, mainly as treatment for musculoskeletal and cutaneous involvement. The authors concluded that treatment was effective in 55% of the patients, based on reduced symptoms and continued use of hydroxychloroquine after 24 weeks. The effectiveness was significantly higher in patients with cutaneous involvement compared to patients with musculoskeletal involvement of sarcoidosis. Side-effects were present in 41.7% of patients leading to cessation of treatment in 21.7% (n=13), mainly due to gastrointestinal side-effects. Hydroxychloroquine has an acceptable tolerance, but prospective studies are needed to confirm efficacy [32].

Finally, two studies aimed to elucidate the aetiology and prognosis of hypersensitivity pneumonitis (HP). Araújo Barros Coelho *et al.* [33] investigated mycological exposure in the home environment in HP patients (n=17) by performing an environmental exposure assessment at home and collecting air samples using an air impactor. The patients reported mould exposure in 47.1% of cases, whilst the home assessment revealed signs of mould in 64.7%. The researchers sampled air from the bedroom of all patients and reported a high prevalence of toxic fungus levels (70.6%). The authors conclude that mould exposure might be underreported in chronic HP. In order to predict treatment response in chronic HP, Lewandowska *et al.* [34] investigated outcomes of immunosuppressive treatment (prednisone and/or azathioprine) in patients with chronic HP. The most prominent predictors for treatment response were fever after antigen exposure, a high lymphocyte count in the bronchial alveolar lavage fluid (>54%), residual volume/total lung capacity >120% predicted and ill-defined nodules on HRCT. Increased eosinophils in bronchoalveolar lavage fluid and fibrosis on HRCT were predictors of a worse prognosis.

Rare ILDs/DPLDs

The 2022 ERS Congress programme included a wide variety of studies in rare ILDs. Studies were mainly focused on biomarkers, (novel) imaging techniques, clinical characteristics, radiological manifestations and respiratory physiology of different rare ILDs.

A French retrospective cohort study, which was granted the award for best abstract of the assembly, looked at pleuroparenchymal manifestations of the recently identified VEXAS syndrome. VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is a monogenic disease of adulthood caused by somatic mutations in *UBA1* in haematopoietic progenitor cells. This study included 114 patients, of whom 45 had pulmonary involvement as assessed by computed tomography (CT). Of these patients, 44% had dyspnoea, 40% cough and 6% needed supplemental oxygen. The three main findings on chest CT were ground-glass opacifications (87%), septal lines (51%) and consolidation (49%); an organising pneumonia pattern was most common. Almost all patients were treated with diuretics and antibiotics with no clear benefit, but they improved with prednisolone (>20 mg). None of the patients developed pulmonary fibrosis [35].

A cross-sectional study from Spain investigated diagnostic accuracy of different biomarkers related to extracellular matrix remodelling and angiogenesis to diagnose lymphangioleiomyomatosis (LAM). This study included patients with LAM, other cystic lung diseases, and healthy controls. MMP-2 and vascular endothelial growth factor (VEGF)-D levels were significantly higher in LAM, compared to other cystic lung diseases and healthy controls. Of note, MMP-2 and VEGF-D levels remained elevated in a subgroup of patients with LAM who underwent a lung transplantation, and were independent of sirolimus treatment.

MMP-2 and VEGF-D in combination showed a diagnostic sensitivity of 79% and specificity of 86%. This was significantly higher than VEGF-D or MMP-2 alone. The study concluded that a combination of MMP-2 and VEGF-D is a potential new diagnostic biomarker for LAM. Further longitudinal studies are needed to confirm the usefulness of MMP-2 in clinical practice [36]. An Irish study in 43 patients with LAM analysed the utility of cyst burden on CT, calculated with a fully automated post-processing tool. They found that cyst burden correlated with VEGF-D, forced expiratory volume in 1 s (FEV_1) and D_{LCO} [37].

A European, multi-centre, observational, retrospective study evaluated outcomes of COVID-19 in patients with pulmonary alveolar proteinosis (PAP) in the pre-vaccination era. All 255 patients with PAP from 11 European referral centres were included in the analysis; 34 (13.3%) patients developed COVID-19. Of these patients, 11 were hospitalised, five were admitted to the intensive care unit and three died or underwent lung transplantation. These patients had a lower D_{LCO} and pulmonary hypertension. The study concluded that the prevalence of COVID-19 among patients with PAP was similar to the general population; however, PAP patients with COVID-19 had increased rates of hospitalisation and death [38].

A French study looked at different trajectories of FEV_1, their determinants and their association with survival in patients with pulmonary Langerhans cell histiocytosis. In this prospective study, 191 patients (age 39±12 years, 59% female, 96% current smokers) were followed for a median time of 5.1 years. Most patients (82%) had stable FEV_1 with minimal annual variation (0.2% of predicted FEV_1). A small group of patients (18%) followed a different trajectory, with an annual FEV_1 decline of 1.8% predicted, and higher mortality. A history of pneumothorax and a higher cystic score at diagnosis were associated with decline in FEV_1. Duration of smoking was not significantly different between the two groups [39].

A French multicentre, retrospective study analysed outcomes in 51 patients with rapidly progressive ILD secondary to anti-MDA5 dermatomyositis. 1-year transplant-free survival was 37% in the whole cohort and only 12% in patients who required mechanical ventilation. 49% of the patients received plasma exchange; these patients were more often treated with immunosuppressants and more often required mechanical ventilation. In a multivariable analysis, only mechanical ventilation was associated with transplant-free survival [40].

A single-centre Irish study provided insights into diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH). The most prevalent symptom was cough, in 50% of patients, but a subgroup of patients was asymptomatic. Sub-centimetre nodules were reported in 90% of patients, mosaic attenuation in one-third and bronchial wall thickening in 10%. Using these three features, novel CT software was used to establish a model, which had an area under the curve of 0.97 for identifying DIPNECH. In 10 histopathological samples, the authors found evidence of increased mechanistic target of rapamycin (mTOR) signalling in DIPNECH. A phase II clinical trial has been designed to evaluate the role of inhaled mTOR inhibitors (sirolimus) in DIPNECH [41].

Concluding remarks

This article summarises a selection of highlights in idiopathic interstitial pneumonias, ILDs of known origin, sarcoidosis and rare ILDs, presented at the ERS Congress 2022. Several RCTs for pharmacological and nonpharmacological treatment of ILDs showed promising (interim) results. Moreover, the meeting provided novel information about disease behaviour of different ILDs and potential (bio)markers to predict disease progression and mortality.

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References

1 Randall M, De Bernard S, Seghers I, *et al.* Assessment of a relationship between prognostic biomarkers and treatment response in ISABELA1&2 IPF cohorts. *Eur Respir J* 2022; 60: Suppl. 66, 846.
2 van der Vis J, Prasse A, Renzoni E, *et al.* Association of MUC5B rs35705950 minor allele with age and survival in European patients with idiopathic pulmonary fibrosis. *Eur Respir J* 2022; 60: Suppl. 66, 1044.
3 Moor CC, Oppenheimer JC, Nakshbandi G, *et al.* Exhaled breath analysis by use of eNose technology: a novel diagnostic tool for interstitial lung disease. *Eur Respir J* 2021; 57: 2002042.
4 van der Sar IG, Moor CC, Vellekoop BP *et al.* Predicting treatment response in patients with interstitial lung disease using electronic nose technology. *Eur Respir J* 2022; 60: Suppl. 66, 345.
5 Myall K, Martinovic J, Wu Z, *et al.* Nocturnal hypoxaemia is associated with mortality in patients with fibrotic interstitial lung disease. *Eur Respir J* 2022; 60: Suppl. 66, 1355.
6 Goos T, Vermant M, De Sadeleer LJ, *et al.* Family history of ILD predicts pulmonary function decline in IPF patients. *Eur Respir J* 2022; 60: Suppl. 66, 2341.
7 Marijic P, Schwarzkopf L, Maier W, *et al.* Outcomes of patients managed in specialized compared to non-specialised ILD centres. *Eur Respir J* 2022; 60: Suppl. 66, 163.
8 Richeldi L, Azuma A, Cottin V, *et al.* Trial of a preferential phosphodiesterase 4B inhibitor for idiopathic pulmonary fibrosis. *N Engl J Med* 2022; 386: 2178–2187.
9 Richeldi L, Azuma A, Cottin V, *et al.* Additive effect of BI 1015550 and nintedanib in patients with IPF. *Eur Respir J* 2022; 60: Suppl. 66, 4606.
10 Maher T, Ganslandt C, Batta R, *et al.* Interim results from AIR, an open-label, single arm, 36–week ph 2 trial of C19 in subjects with idiopathic pulmonary fibrosis. *Eur Respir J* 2022; 60: Suppl. 66, 4402.

11 Deterding R, Young LR, Deboer EM, *et al.* Nintedanib in children and adolescents with fibrosing interstitial lung disease: the InPedILD trial. *Eur Respir J* 2022; 60: Suppl. 66, 621.
12 Maher TM, Forbes W, Bortey E, *et al.* An interim analysis of a phase 2 trial evaluating oral nalbuphine extended release for treating chronic cough in idiopathic pulmonary fibrosis. *Eur Respir J* 2022; 60: Suppl. 66, 4404.
13 Edwards GD, Polgar O, Patel S, *et al.* Anxiety and Depression in IPF and response to pulmonary rehabilitation (PR). *Eur Respir J* 2022; 60: Suppl. 66, 518.
14 Samuel Santos E, Rodrigues G, Souto-Miranda S, *et al.* Anxiety and depression symptoms after pulmonary rehabilitation in people with interstitial lung disease: responders and non-responders. *Eur Respir J* 2022; 60: Suppl. 66, 3523.
15 Breuls S, Blondeel A, Wuyts M, *et al.* Physical activity coaching in patients with ILD: a pilot study. *Eur Respir J* 2022; 60: Suppl. 66, 2447.
16 Distler O, Highland KB, Gahlemann M, *et al.* Nintedanib for systemic sclerosis-associated interstitial lung disease. *N Engl J Med* 2019; 380: 2518–2528.
17 Wells A, Wuyts WA, Gläser S, *et al.* Effects of nintedanib in patients with systemic sclerosis-associated ILD (SSc-ILD) and differing levels of lung function impairment. *Eur Respir J* 2022; 60: Suppl. 66, 475.
18 Kreuter M, Denton CP, Ho LA, *et al.* Progression of systemic sclerosis-associated ILD (SSc-ILD) and effect of nintedanib in subgroups by monocyte and neutrophil counts. *Eur Respir J* 2022; 60: Suppl. 66, 608.
19 Guler SA, Sarbu A, Stadler O, *et al.* Persistent inflammation in systemic sclerosis is strongly associated with mortality: a EUSTAR database analysis. *Eur Respir J* 2022; 60: Suppl. 66, 1912.
20 Hoffmann-Vold AM, Brunborg C, Airò P, *et al.* Cohort enrichment strategies for progressive interstitial lung disease in systemic sclerosis from EUSTAR. *Eur Respir J* 2022; 60: Suppl. 66, 1100.
21 Njock M, Henket M, Jacquerie P, *et al.* Plasma-derived exosomal miRNAs as non-invasive biomarkers for lung involvement in systemic sclerosis. *Eur Respir J* 2022; 60: Suppl. 66, 2918.
22 Stock C, Seeliger B, Cameli P, *et al.* Extensive autoantibody panel in systemic sclerosis associated interstitial lung disease. *Eur Respir J* 2022; 60: Suppl. 66, 2922.
23 Solomon JJ, Danoff SK, Woodhead FA, *et al.* Safety, tolerability, and efficacy of pirfenidone in patients with rheumatoid arthritis-associated interstitial lung disease: a randomised, double-blind, placebo-controlled, phase 2 study. *Lancet Respir Med* 2022; 11: 87–96.
24 Perrot M, Ghaye B, Zan D, *et al.* Lung involvement in early rheumatoid arthritis, interim analysis of the FINDRA prospective study. *Eur Respir J* 2022; 60: Suppl. 66, 1664.
25 Bonella F, Vegas Sanchez MC, Castillo Villegas D, *et al.* Serum KL-6 improves prediction of progressive phenotype (PP) at one year independently of underlying interstitial lung disease (ILD): results from the VAMOS study. *Eur Respir J* 2022; 60: Suppl. 66, 1274.
26 Cocconcelli E, Zanatta E, Bellani S, *et al.* Predictors of interstitial lung disease (ILD) in patients with idiopathic inflammatory myopathy-associated (IIM). *Eur Respir J* 2022; 60: Suppl. 66, 3074.
27 Terschluse C, Feineis M, Meschede W, *et al.* Bronchoscopy in sarcoidosis – EBUS-TBNA, transbronchial biopsy or cryobiopsy? *Eur Respir J* 2022; 60: Suppl. 66, 2278.
28 Raniszewska A, Rutkowska E, Kwiecien I, *et al.* Imbalance between Th17 and Tregs in the EBUS/TBNA lymph nodes in patients with pulmonary sarcoidosis. *Eur Respir J* 2022; 60: Suppl. 66, 2273.
29 Jeny F, Cumin M, Khafagy P, *et al.* Changes in forced vital capacity over time in pulmonary fibrosis sarcoidosis: application of group-based trajectory modelling. *Eur Respir J* 2022; 60: Suppl. 66, 2926.
30 Cameli P, Pastore MC, Mandoli GE, *et al.* Strain echocardiography for the prognostic estimation of patients with sarcoidosis. *Eur Respir J* 2022; 60: Suppl. 66, 200.
31 Kahlmann V, Moor CC, Van Helmondt SJ, *et al.* Online mindfulness-based cognitive therapy reduces anxiety and depression in patients with sarcoidosis. *Eur Respir J* 2022; 60: Suppl. 66, 888.
32 Vermeer B, Veltcamp M, Vorselaars AD, *et al.* Effect of hydroxychloroquine in cutaneous sarcoidosis or musculoskeletal-related pain. *Eur Respir J* 2022; 60: Suppl. 66, 763.
33 Araújo Barros Coelho DJ, Rufo JC, Santos RF, *et al.* Home environmental fungal exposure in patients with hypersensitivity pneumonitis – pilot analysis. *Eur Respir J* 2022; 60: Suppl. 66, 4281.
34 Lewandowska KB, Baranska I, Sobiecka M, *et al.* Chronic hypersensitivity pneumonitis – how to predict treatment success? *Eur Respir J* 2022; 60: Suppl. 66, 3131.
35 Borie R, Debray MP, Audemard A, *et al.* Pleuropulmonary manifestations of VEXAS syndrome. *Eur Respir J* 2022; 60: Suppl. 66, 104.
36 Revilla Lopez EM et al Exploring the role of matrix metalloproteinase 2 (MMP-2) as biomarker in lymphangioleiomyomatosis. *Eur Respir J* 2022; 60: Suppl. 66, 144.
37 Lynn E, Ocallaghan M, Morrow J, *et al.* Cyst burden on high-resolution computed tomography (HRCT) correlates with VEGF-D in lymphangioleiomyomatosis. *Eur Respir J* 2022; 60: Suppl. 66, 3896.
38 Papiris S, Campo I, Mariani F, *et al.* COVID-19 in patients with pulmonary alveolar proteinosis. A European multicenter study. *Eur Respir J* 2022; 60: Suppl. 66, 328.

39 Benattia A, Porcher R, Bugnet E, *et al.* Two distinct trajectories of FEV_1 in Adult Pulmonary Langerhans Cell Histiocytosis. *Eur Respir J* 2022; 60: Suppl. 66, 2780.
40 Bay P, Pineton de Chambrun M, Vincent R, *et al.* Plasma exchange are not associated with better outcome in MDA5 rapidly-progressive interstitial lung disease. *Eur Respir J* 2022; 60: Suppl. 66, 2397.
41 O'Callaghan M, Almeamar H, Gleeson M, *et al.* A DIPNECH deep dive. *Eur Respir J* 2022; 60: Suppl. 66, 2599.