Young Investigator Group (YIG)

EULAR highlights

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2. SYSTEMIC SCLEROSIS HIGHLIGHTS – CLINICAL ASPECTS OF SYSTEMIC SCLEROSIS – IMAGING AND BIOMARKERS

By Stefano Di Donato

The presentations from this session offered valuable insights into the role of biomarkers and advanced imaging techniques in systemic sclerosis. From lung ultrasound (LUS) and magnetic resonance imaging (MRI) to diffusion capacity of carbon monoxide (DLCO) changes and interferon (IFN) scores, these tools are pushing the boundaries of how we understand and manage systemic sclerosis (SSc), offering new hope for earlier detection, better risk stratification, and more effective treatment of this complex disease.

Echoes beneath the surface

Unveiling the hidden depths of lung ultrasound in SSc-ILD.

The work presented by Dr. Mohammad Reza Beigi from Sapienza University of Rome demonstrated that LUS can potentially overcome its traditional limitations in detecting interstitial lung disease (ILD) in SSc. By comparing LUS B-lines and pleural line alterations (PLA) with automated quantitative computed tomography (qCT), the study revealed significant correlations between LUS scores and qCT findings. LUS was able to reflect structural changes in the lung surface and even, to some extent, deeper lung tissues. The strongest associations were found in the basal lung fields, where SSc-ILD is most prevalent. This is a crucial finding as it suggests that LUS, particularly using the PLA scoring system developed at the research center, could provide a reliable and non-invasive alternative to qCT for tracking lung involvement in SSc. This work could help clinicians better monitor lung disease in SSc patients while minimizing the need for more expensive and radiation-exposing procedures like CT scans.

Signals from the silent brain

Decoding deep white matter changes in SSc.

Another significant study from China, led by Dr. Xu of Peking Union Medical College Hospital, focused on the brain involvement in SSc. Using MRI, Dr. Xu's team identified deep white matter hyperintensities (DWMHs) in SSc patients, which were more prevalent compared to healthy controls. The study revealed that these hyperintensities, which are thought to result from ischemia or hypoperfusion, might reflect early vascular changes in the central nervous system. Notably, the volume ratios of DWMHs to whole white matter were significantly higher in SSc patients, suggesting that DWMHs could serve as an early marker of CNS involvement in SSc before the appearance of clinical symptoms. The study offers insight into the often-overlooked neurological aspects of SSc and proposes DWMHs as a possible biomarker for early CNS monitoring in these patients.

Breathing between the lines

Tracking DLCO changes to predict survival in SSc-associated PAH.

Dr. Fretheim from Oslo University Hospital presented a study on pulmonary arterial hypertension (PAH) in systemic sclerosis. The team investigated the prognostic value of changes in diffusion capacity of carbon monoxide (DLCO) over a 12-month period after PAH diagnosis. They found that changes in DLCO, especially improvements, were linked to better survival outcomes. Patients whose DLCO improved over the year had a significantly higher survival rate compared to those with stable or worsening DLCO values. This finding supports the inclusion of DLCO measurements in risk stratification models for SSc-associated PAH, indicating that DLCO changes can be an early predictor of patient outcomes. This study underscores the importance of DLCO as a dynamic marker, rather than a static measurement, in monitoring disease progression and guiding treatment strategies in PAH-SSc patients.

The fibrosis lockdown on CT scans

Nintedanib's role in slowing lung damage in SSc-ILD as assessed by CT scans.

Dr. Di Battista from the University of Pisa focused on the effects of the antifibrotic drug Nintedanib in patients with SSc-associated interstitial lung disease (SSc-ILD). Using high-resolution computed tomography (HRCT) alongside quantitative post-processing software, the team assessed changes in lung fibrosis over time. Their findings showed that patients treated with Nintedanib experienced stabilization in almost all lung parameters, unlike those who did not receive antifibrotic treatment, who showed a significant worsening in lung fibrosis. Interestingly, the study highlighted that pulmonary vascular-related structures (VRS) worsened even in patients receiving Nintedanib, suggesting a need for further investigation into how vascular disease progresses in SSc-ILD despite antifibrotic therapy. This study adds valuable data to the body of evidence supporting Nintedanib's role in slowing fibrosis progression in SSc-ILD, while also raising questions about the management of vascular involvement in these patients.

2.1 The silent autoantibodies

Anti-Ro52 antibodies: markers of unseen risk in SSc.

Dr. Martel and her colleagues from Lille University presented a systematic review and meta-analysis on the prevalence and clinical significance of anti-Ro52/TRIM21 antibodies in systemic sclerosis. Their meta-analysis, which included data from over 11,000 SSc patients, revealed that anti-Ro52 antibodies are present in approximately 23% of patients and are significantly associated with a higher risk of pulmonary arterial hypertension (PAH), interstitial lung disease (ILD), and Sjögren's syndrome. The team's own cohort study mirrored these findings, showing that anti-Ro52-positive patients were more likely to develop severe cardio-pulmonary complications. This research highlights the importance of screening for anti-Ro52 antibodies in SSc patients, as their presence could help identify those at higher risk for complications and guide more personalized monitoring and treatment strategies.

2.2 The heart speaks in code

Decoding the cardiac MRI patterns that predict survival in SSc.

The work of Dr. Cerasuolo from the Catholic University of the Sacred Heart in Rome delved into cardiac involvement in systemic sclerosis, an often underdiagnosed but life-threatening complication of the disease. Using cardiac magnetic resonance imaging (CMR), the study classified patients into five distinct cardiac phenotypes and explored the associations between these phenotypes, myocardial markers, and long-term survival. The study found that patients with right ventricular failure (RVF) and large cardiac cavities had significantly worse survival rates compared to those with normal cardiac function. Additionally, higher levels of NT-proBNP and more frequent ventricular ectopic beats were noted in these high-risk groups. The findings confirmed that CMR phenotyping is a powerful tool for predicting outcomes in SSc patients with cardiac involvement and underscored the need for early identification and monitoring of these at-risk patients.

The Interferon whisper

A novel score that predicts outcomes in limited cutaneous systemic sclerosis.

Finally, Dr. Di Donato from the University of Leeds presented a novel approach to risk stratification in limited cutaneous SSc using interferon (IFN) score. By analyzing serum levels of six IFN-inducible chemokines, the team found that patients with higher IFN scores were more likely to experience severe clinical outcomes, including PAH, finger gangrene, scleroderma renal crisis, SSc-related death, and new onset or progression of existing ILD. This study offers a new biomarker that could be integrated into clinical trials and patient management to better predict disease progression in lcSSc. By identifying high-risk patients earlier, clinicians could tailor treatments and interventions more effectively, potentially improving long-term outcomes in this subset of SSc patients.

3. SYSTEMIC SCLEROSIS HIGHLIGHTS – CLINICAL ASPECTS OF SYSTEMIC SCLEROSIS – CLINICAL STUDIES

By Devis Benfaremo

Each presentation of this session has dived deep into the complex scenario of systemic sclerosis with various organ systems, and as a global vascular disease, revealing new insights into management and prognosis.

3.1 The Silent Lung Threat

Uncovering the risk of Interstitial Lung Disease in systemic sclerosis.

Dr Liubov Petelytska and coworkers presented the study: "Incidence and risk factors for new onset interstitial lung disease in systemic sclerosis: insights from an analysis of the EUSTAR cohort", in which they enrolled 5331 SSc patients without lung involvement at baseline, observing an ILD incidence rate of 3.7 cases per 100 person-years. Importantly, the annual incidence was stable for up to 10 years. They also identified the following risk factors to develop new onset ILD: dyspnea NYHA stage≥2 (HR 1.23, 95% CI 1.08-1.40), male sex (HR 1.28, 95% CI 1.10-1.50), age (HR 1.02, 95% CI 1.01-1.02), elevated inflammatory markers (HR 1.59, 95% CI 1.35-1.87), anti-topoisomerase I antibody (HR 2.15, 95% CI 1.82-2.53), and digital ulcers ever (HR 1.77, 95% CI: 1.49-2.08). These results reinforce the importance of continuing ILD screening in SSc patients without lung involvement at baseline, especially in patients with one or more risk factors.

3.2 Hidden Dangers Beneath the Surface

The impact of comorbidities on the prognosis of systemic sclerosis patients.

Dr Cosimo Bruni, on behalf of his coworkers and Martina Orlandi, presented the study: "Towards a comprehensive approach to the management and prognosis of systemic sclerosis patients: the role of comorbidities in the SPRING-SIR registry", showing that among 1910 SSc patients 67.3% presented with at least one comorbidity at baseline, the most frequent being systemic arterial hypertension (23.7%) osteoporosis (12.9%) and dyslipidemia (11%). Patients with mild of no comorbidities were more frequently ATA+, diffuse SSc, with shorter disease duration, with lower prevalence of cardiopulmonary involvement and pulmonary functional tests impairment, but a higher prevalence of peripheral vasculopathy, whereas patients with higher comorbidity burden were more frequently ACA+, limited SSc with longer disease duration, with more frequent cardiopulmonary involvement both in terms of ILD and PAH, determining more frequent dyspnoea and lower PFT values. Finally, the comorbidity score and the baseline EUSTAR activity index significantly and independently increased the risk of death over time.

3.3 The Reproductive Clock Ticks Faster

Exploring ovarian dysfunction in women with systemic sclerosis.

In her groundbreaking study, Dr. Liyi Dai delved into the reproductive health challenges faced by women with SSc. The research involved comparing 44 SSc patients to 44 healthy controls, with a focus on measuring anti-Müllerian hormone (AMH) levels as an indicator of ovarian reserve. The study found significantly lower AMH levels in SSc patients, pointing to an accelerated decline in ovarian function, particularly in women over 30. SSc patients also reached perimenopause earlier than controls, highlighting the disease's impact on fertility. The study emphasizes the importance of early reproductive health counseling and monitoring in women with SSc, offering new insights into managing fertility issues in this population.

3.4 A Fragile Heart: Systemic Sclerosis and Cardiac Involvement

Identifying the hidden risks of primary heart disease in systemic sclerosis.

Cardiac involvement is a leading cause of death in systemic sclerosis, and Dr. Andrea-Hermina Györfi et al used the EUSTAR database to evaluate SSc primary heart involvement (SSc-pHI), defined according to the 2022 consensus-based WSF/HFA definition. Among 5741 SSc patients, muscle atrophy (OR 2.00), age (OR 1.91), male sex (OR 1.77), swollen joints (OR 1.70), muscle weakness (OR 1.38), and tendon friction rubs (OR 1.36) were identified as risk factors for the presence of SSc-pHI, whereas telangiectasia (OR 2.10), intestinal symptoms (OR 1.70), age (OR 1.47), and Scl-70 antibodies (OR 1.37) were associated with an increased risk for the development of SSc-pHI. Swollen joints were associated with an increased risk of progressive SSc-pHI (OR 2.49). Finally, the overall survival rate of patients with SSc-pHI was significantly lower than of patients without SSc-pHI. These results should inform those who follow SSc patients on the importance of detecting either clinical or subclinical heart involvement.

3.5 Gut Instinct: Diagnosing Intestinal Involvement in Systemic Sclerosis

New insights into small intestinal dysmotility using high-resolution manometry.

In a novel approach to understanding gastrointestinal involvement in SSc, Dr. Luis Gerardo Alcala-Gonzalez and coworkers presented the study: "Categorization of Small Intestinal Involvement in Systemic Sclerosis Using High-Resolution Jejunal Manometry". Using a 35-channel high-resolution manometry catheter, they recorded small intestinal motility for 3 hours fasting and 2 hours during continuous nutrient perfusion at 2 kcal/min. Twenty patients with SSc showed reduced motor activity during fasting compared to healthy volunteers, secondary to a significant reduction in propagated contractile fronts of the small intestine. During nutrient infusion, patients with SSc showed decreased motor activity mainly due to an abnormal response to nutrients. Assessing criteria for intestinal dysmotility, 13 (65%) patients fulfilled abnormal patterns compatible with intestinal dysmotility (6 patients exhibited a neuropathic pattern and 7 patients a myopathic pattern). Interestingly, neither

esophageal aperistalsis nor gastroparesis were significant predictors of intestinal dysmotility. This study highlights that using non or minimally invasive techniques may be useful for assessing GI symptoms in SSc patients but also for characterizing the heterogeneity of GI involvement, hopefully paving the way for novel therapeutic approaches.

3.6 Inflammation's Unforgiving Grip

The prognostic value of C-reactive protein in systemic sclerosis.

Persistent inflammation plays a critical role in systemic sclerosis outcomes, as Dr. Carlos Sieiro Santos highlighted in his study on C-reactive protein (CRP)-associated phenotypes. The research involved 133 SSc patients, with 39% showing persistently high CRP levels. These patients were more likely to have diffuse-cutaneous disease, anti-Scl70 antibodies, and interstitial lung disease (ILD). Additionally, they faced a 4.6-fold higher risk of mortality and a 5.6-fold higher risk of ILD development compared to non-inflammatory patients. The findings suggest that monitoring CRP levels over time could help identify patients at higher risk for severe disease manifestations, allowing for earlier intervention and more tailored treatment strategies.

3.7 The Vascular Puzzle in Systemic Sclerosis

Developing a unified vascular endotype for predicting outcomes in systemic sclerosis.

Dr. Stefano Di Donato's study tackled the challenge of predicting vascular complications in systemic sclerosis by proposing a Unified Vascular Phenotype (UVP) score. Among 8958 included patients, the unified vascular phenotype (UVP) score, composed of presence of telangiectasia, pitting scars, puffy fingers, and history of DUs, was significantly associated with an increased risk of mortality (HR 1.67; C.I. 95% 1.47-1.89, $p<0.001$) after adjusting for age, gender, Leroy subset, ESR, raised CRP, anti-Topoisomerase I, anti-Centromere, baseline FVC (%), presence of dyspnea, baseline DLCO (%), PAH, and disease duration. Other covariates significantly associated with mortality in the model included ESR, male gender, age, and PAH. UVP score was also significantly associated with an increased hazard of developing a combined vascular endpoint – including PAH, heart failure, scleroderma renal crisis, and finger gangrene (HR 1.17, 95% C.I. 1.08-1.27, $p<0.001$) after adjusting for the same variables used in survival analysis. The prognostic value of this unified vascular score can inform clinical trial enrichment strategies and may be also useful for the implementation of stratified approaches for clinical management.

3.8 Predicting Stability in the Unpredictable World of ILD

Long-term stability of interstitial lung disease in systemic sclerosis depends on the definition of progression.

In her detailed analysis, Prof. Anna-Maria Hoffmann-Vold et al explored the concept of "Prediction of stable SSc-ILD". Among 231 SSc-ILD patients included, 75 (32%) had stable ILD over three years defined by no FVC decline ≥5%, 133 (58%) defined by not fulfilling the PPF guidelines criteria and 105 (45%) not fulfilling the INBUILD PF-ILD criteria. Interestingly, stable ILD using no FVC ≥5% decline was predicted by lower baseline FVC, while stable ILD defined by no PPF and no PF-ILD was significantly predicted by the absence of dcSSc and of ground glass opacities on HRCT. This study highlights that long-term stable ILD in SSc occurs, but the frequency varies based on which definition is applied. Prediction of stable patients is challenging, highlighting the necessity of comprehensive disease assessment and monitoring over time.

4. SYSTEMIC SCLEROSIS POSTER TOUR – SESSION I

By Elena Cristina Nita

The following abstracts were provided were presented during the Clinical Poster Tour, Session I, at EULAR 2024. Topics range from gastrointestinal and pulmonary complications to the development of prognostic biomarkers, each offering a glimpse into the future of SSc management and therapy.

4.1 Nita C. et al - Disease burden and impact of fecal incontinence in systemic sclerosis – reSScue trial data.

This poster addresses the often-overlooked burden of fecal incontinence (FI) in SSc. The ReSScue trial evaluated 67 SSc patients with lower gastrointestinal (GI) symptoms, focusing on FI prevalence using two patient-reported outcome measures (FIQL and UCLA GIT). FI was more commonly identified using the FIQL scale, revealing that 72% of patients had FI, while 33% were identified by the UCLA GIT. Associations were found between severe FI and digital ulcers, diarrhoea, and skin involvement, suggesting that early FI detection is critical in improving quality of life for SSc patients.

4.2 Hoffmann-Vold et al. - evidence-based expert consensus definition of organ involvement in systemic sclerosis – a EUSTAR study.

This study, led by Hoffmann-Vold et al., establishes consensus definitions for SSc organ involvement. By reviewing 820 papers, 179 definitions were identified, and 199 items were proposed for defining the involvement of lungs, heart, skin, kidneys, and more. A total of 74 tools were endorsed to describe organ severity, progression, and improvement. These data-driven definitions are essential for standardizing clinical trials and improving the assessment of SSc disease behavior. The definitions aim to enhance research consistency and patient outcome comparison across multiple studies.

4.3 Assassi et al. - Prognostic value of circulating biomarkers in systemic sclerosis-associated interstitial lung disease (SSc-ILD).

This work by Assassi et al. investigates the role of specific biomarkers, including KL-6, CRP, and CCL2, in predicting the progression of SSc-ILD. Using data from the SENSCIS trial, researchers found that elevated KL-6 levels were associated with faster forced vital capacity (FVC) decline, while higher CRP and CCL2 levels predicted worsening skin fibrosis over 52 weeks. These findings suggest that measuring these biomarkers could help identify patients at higher risk of disease progression, allowing for earlier intervention in SSc-ILD and better management of lung and skin complications. This will have also implications for clinical trials enrichment.

Bjørkekjær et al. - PAH treatment at time of diagnosis is associated with improved survival regardless of hemodynamic thresholds and risk stratification – A EUSTAR analysis.

This EUSTAR analysis by Bjørkekjær et al. highlights the importance of upfront treatment for pulmonary arterial hypertension (PAH) in SSc. By comparing patients who received PAH treatment at diagnosis to those who didn't, the study found that those without treatment had worse survival rates. Even patients with milder hemodynamic involvement benefited from early intervention, supporting the recommendation for upfront PAH therapy, independent of risk stratification or existing conditions. The results underscore the need for timely PAH management in SSc to improve long-term outcomes.

4.4 Cutolo et al. - Mapping dermal thickness and skin hardness in healthy individuals by high-frequency sonography and durometry.

Cutolo et al. present a pilot study that maps dermal thickness and skin hardness in healthy individuals using high-frequency sonography and durometry. By comparing data from different age groups and geographic regions, the study establishes normal values for skin measurements. The data will serve as a baseline for assessing skin fibrosis in SSc patients, improving diagnostic precision. Significant variations in skin hardness and thickness were found across body areas, sex, and age groups, which may aid in the clinical evaluation of fibrotic skin in SSc.

4.5 Hoffmann-Vold et al. - Milder ILD with preserved lung function significantly contributes to respiratory-caused mortality in systemic sclerosis.

This analysis by Hoffmann-Vold et al. from the Norwegian SSc cohort explores the contribution of milder ILD to respiratory mortality in SSc patients. Surprisingly, even those with preserved lung function (FVC ≥70%) faced significant risk of respiratory death, primarily due to respiratory infections. Older age, male sex, and pulmonary hypertension were associated with higher mortality. These findings emphasize that milder ILD can still lead to severe outcomes, indicating a need for vigilant monitoring and early treatment to improve survival in SSc-ILD patients.

4.6 Hoffmann-Vold et al. - Prognostic value of change in forced vital capacity (FVC) at week 12 or 24 in autoimmune disease-related ILD.

Hoffmann-Vold et al. assess whether short-term changes in FVC can predict long-term outcomes in patients with autoimmune disease-related ILD, including SSc. Using data from the SENSCIS and INBUILD trials, researchers found that changes in FVC at weeks 12 and 24 were moderately correlated with FVC at 52 weeks. This finding suggests that early FVC changes may help predict disease progression and overall lung decline trajectory. This in turn will inform treatment decisions, allowing clinicians to adjust therapeutic strategies sooner in patients with progressive ILD.

4.7 Roth et al. - Characteristics and disease course of SSc-ILD patients with gastroesophageal reflux – A EUSTAR cohort study

Gastroesophageal reflux disease (GERD) is common in patients with SSc-ILD, and this study by Roth et al. evaluates its impact on disease progression. GERD was reported in over 80% of SSc-ILD patients and was associated with worse lung function, lower FVC, and more severe respiratory symptoms. Predictors of ILD progression included older age, female sex, and use of ILD-modifying drugs. GERD's persistent and severe nature, particularly in those on proton pump inhibitors, was associated with increased mortality and ILD progression, emphasizing the need for targeted GERD management in these patients, as well as how the involvement of the oesophagus can be more prevalent in severe disease phenotypes.

4.8 Bruni et al. – New-onset ILD in systemic sclerosis: clinical course and outcomes from a EUSTAR database analysis

Bruni et al. present this EUSTAR analysis comparing SSc patients with new-onset ILD to those with pre-existing ILD and ILD-negative patients. Patients with incident (new-onset) ILD had milder functional impairment at baseline and lower mortality than those with ILD at diagnosis but worse outcomes than ILD-negative patients. The study shows that also new-onset ILD can lead to significant functional decline and mortality. Continued screening for ILD during SSc follow-up is essential for early detection and timely intervention to improve patient outcomes.

5. SYSTEMIC SCLEROSIS HIGHLIGHTS – CLINICAL ASPECTS OF SYSTEMIC SCLEROSIS – TREATMENT

By Stefano Di Donato

In this session diverse and cutting-edge approaches investigated in systemic sclerosis (SSc) treatment were presented, offering new insights into both personalized medicine and innovative therapeutic strategies.

5.1 Pushing the limits: stem cell transplantation for systemic sclerosis

New hope for patients with heart or lung involvement

In this prospective phase II study, A.C. Pecher and colleagues explored autologous hematopoietic stem cell transplantation (aHSCT) as a treatment for progressive SSc in patients with either lung or heart involvement. The study aimed to assess both the feasibility and safety of aHSCT in a population considered high-risk due to severe organ involvement. Patients were stratified according to their specific manifestations and received a reduced cyclophosphamide mobilization regimen. Results showed that while the treatment had significant overall survival benefits (60% at 36 months), the transplant-related mortality rate was unexpectedly high at 11.4%, particularly in patients with cardiac involvement. Despite these risks, aHSCT led to significant improvements in skin and lung function, suggesting its potential as a life-saving treatment option for select SSc patients.

5.2 Shifting paradigms: changing treatment patterns in SSc-ILD

Real-world data on treatment evolution from the EUSTAR cohort

C. Campochiaro and collaborators investigated changes in immunosuppressive treatment use and its effect on patients with SSc-interstitial lung disease (ILD) from the EUSTAR cohort. The study analyzed 1,409 patients across four time periods, revealing that IST use increased from 13.6% to 57.4% between 2006 and 2017. The introduction of novel therapies and combination regimens significantly improved outcomes, with fewer progressive ILD events and improved progression-free survival, particularly in anti-topoisomerase I positive patients. While treatment advances have reduced disease progression, challenges remain, as nearly half of patients still experience disease progression at 3 years, underscoring the need for continued innovation in treatment approaches.

5.3 Protecting the heart and lungs: Ambrisentan's role in pulmonary arterial hypertension prevention

Long-term effects of early pulmonary hypertension treatment in SSc

In this study, P. Xanthouli and colleagues extended the findings of the EDITA trial by assessing the long-term benefits of ambrisentan, an endothelin receptor antagonist, in SSc patients with mild pulmonary arterial hypertension (PAH). The follow-up data demonstrated that patients treated with ambrisentan

showed significant improvements in pulmonary arterial pressure and were protected from the development of full-blown PAH over a mean follow-up of 2.25 years. Notably, none of the patients receiving ambrisentan developed PAH, compared to four new PAH cases in the control group. These findings support the early use of vasodilative therapy in SSc to prevent disease progression and improve outcomes. Longer follow-up data are awaited with enthusiasm to better understand the disease-modifying ability of endothelin receptor antagonists.

5.4 Gut feeling: faecal microbiota transplantation in SSc

A new frontier in treating gastrointestinal involvement in systemic sclerosis.

C. Nita and team presented results from the ReSScue trial, exploring the efficacy of fecal microbiota transplantation (FMT) for treating moderate to severe lower gastrointestinal symptoms in SSc. Although the primary endpoints of diarrhoea and bloating showed no significant improvement, the exploratory analysis revealed a marked reduction in faecal incontinence symptoms in patients receiving FMT. These improvements were observed after 20 weeks and correlated with better stool consistency. However, no significant changes were noted in the quality-of-life scores, indicating that while FMT may alleviate certain symptoms, its broader impact on gastrointestinal health in SSc requires further study.

5.5 Retention rates of Rituximab: a real-life study

How well does rituximab hold up in treating systemic sclerosis?

In this multicenter real-life study, G. De Luca and colleagues evaluated the retention rates of rituximab in 152 SSc patients over five years. The study found that rituximab had a retention rate of 59.9% after five years, with most discontinuations due to clinical improvement rather than adverse events or treatment failure. Skin and lung function remained stable, particularly in patients with ILD. Rituximab was most effective in patients with short disease duration, anti-Scl70 negativity, and those without arthritis. This long-term data underscores rituximab's safety and efficacy as a treatment option for skin and lung fibrosis in SSc. Particularly as a therapeutic option in the early stages of the disease.

5.6 Lung transplantation for SSc: a lifesaving option

Improving survival and disease control in systemic sclerosis with end-stage lung disease

C. Iannone and her team conducted a multicentre retrospective analysis on SSc patients who underwent lung transplantation (LT) for ILD. The study reported excellent short term survival rates, with 100% survival at one year and 92.3% at two years. In addition to improved lung function, significant reductions in skin fibrosis and disease activity were observed. All patients showed improvement in pulmonary function tests and EUSTAR disease activity scores. This study highlights the potential of LT not only as a life-extending treatment but also as a method to control disease

progression in SSc patients with severe lung involvement. Further studies will be necessary to validate the long-term survival and event-free survival from clinically relevant events in transplanted patients.

5.7 Tocilizumab vs. Rituximab: a battle for the lungs

New data on personalized biologic treatment for SSc-ILD

Akin to what has been pioneered on rheumatoid arthritis, where synovial biopsy-driven treatment has been proposed with relatively successful results. M. Hassanien and colleagues presented a 52-week, biopsy-driven randomized controlled trial comparing the effectiveness of tocilizumab and rituximab in SSc patients with SSc-ILD. Patients were stratified by B-cell poor or B-cell rich lung biopsies. Tocilizumab was found to be more effective in B-cell poor patients, while rituximab outperformed in B-cell rich patients. This study highlights the importance of personalized medicine in SSc, demonstrating that different biologics may work best depending on the underlying lung pathology. Future studies are needed to replicate these findings and validate the use of RNA sequencing for patient stratification.

5.8 Battling the trajectory of skin fibrosis: Rituximab vs. Tocilizumab

Which biologic is better for treating skin fibrosis in systemic sclerosis?

In a comparative study, S. Kubo and colleagues evaluated the effectiveness of rituximab and tocilizumab in reducing skin fibrosis in SSc patients. Over a 24-week period, both biologics showed significant improvements in modified Rodnan skin score (mRSS) compared to standard of care, with no significant difference between the two treatments. Immunophenotyping revealed that rituximab's effectiveness was correlated with a reduction in plasmablasts and different T-cell populations, suggesting that patient-specific immune profiles could guide treatment decisions and identifying a more profound imprinting on the immune system imparted by rituximab. The study concludes that while both therapies are effective, biomarkers may help tailor treatment to individual patient needs.

6. BASIC ABSTRACT SESSIONS - PATHOPHYSIOLOGY IN SYSTEMIC SCLEROSIS DISEASE

By Marco Minerba

Systemic Sclerosis (SSc), also called Scleroderma, is an immune-mediated rheumatic disease characterised by fibrosis of the skin and internal organs and vasculopathy. Improved understanding of underlying pathogenetic mechanisms has allowed better management of the disease, although SSc pathogenesis hasn't been totally elucidated.

Anti-PRMT5: a new marker for SSc diagnosis and progression

Unlocking the potential of anti-PRMT5 antibodies in systemic sclerosis.

New discoveries about SSc pathophysiology have been made recently. Anti-PRMT5 has emerged as a promising autoantibody for SSc diagnosis, having been detected in 31% of SSc patients and resulting absent in healthy controls (sensitivity 70.2%, specificity 97.8%). Elevated levels of anti-PRMT5 antibody may predict disease progression for both skin and lung fibrosis. As for skin, patients with SSc and modified Rodnan Skin Score (mRSS) progression display a numerical elevation in baseline levels of anti-PRMT5 antibodies compared with SSc patients without skin progression. Likewise, patients with SSc fulfilling the criteria of progressive fibrosing interstitial lung disease (PF-ILD) demonstrate significantly increased basal levels of anti-PRMT5 antibodies as compared with the patients with SSc without developing PF-ILD. The title of anti-PRMT5 antibodies could also reflect the inflammatory status in SSc patients, since serum anti-PRMT5 antibodies correlate positively with the levels of acute phase reactants like erythrocyte sedimentation rate (ESR) and C reactive protein (CRP), as well as IgG and tissue inhibitor of metal protease 1 (TIMP- 1).

Unravelling the genetic basis of sex-bias in SSc

Novel loci suggest protective factors in males.

A genetic component involved in SSc sex-bias may explain the differential prevalence (females to males ratio 8:1) and the different clinical manifestations between sexes. This genetic component involves two novel risk loci for the disease, annotated to NRP1 (chromosome 10) and BCL11A (chromosome 2).

NRP1 is a cell membrane protein implicated in immune and vascular functions. In particular, it regulates the function and survival of T regulatory cells and has been found to be decreased in SSc, both in serum and skin biopsies from affected skin.

BCL11A is expressed in hematopoietic stem cells. It has been reported to be essential for B-cells lymphopoiesis and early B cell survival. Moreover, it is necessary for plasmacytoid dendritic cells (pDC) development, main producers of IFN type 1, which show sex-biased function.

Both genes could be protective in males by reducing vascular damage and pDC function, respectively.

A new endothelial cell population in SSc: key to vasculopathy and fibrosis

CD34+, αSMA+, CD31+ cells hold the answer to progressive fibrosis.

A novel vascular endothelial cell population, which is CD34+, αSMA +, CD31+, has been identified.

This new population, located in close proximity to immune cells and myofibroblasts, is increased in SSc skin and expresses markers for endothelial to mesenchymal transition (SNAI1, SNAI2, TWIST1, and ZEB1). On the other side, levels of endothelial precursor cells (defined as CD34+;CD133+;CD31+cells or CD34+;VEGFR2high;CD31+ cells) are remarkably decreased in SSc skin.

CD34+,αSMA+,CD31+ VEC counts are associated with clinical outcomes of progressive fibrotic remodelling, thus providing a novel cellular correlate for the crosstalk of vasculopathy and fibrosis.

Anti-topoisomerase autoantibodies: dual effects on macrophage function

The complex role of anti-topoisomerase autoantibodies in SSc inflammation.

Emerging data are explaining the role of ATA (anti-topoisomerase autoantibodies) in the pathogenesis of SSc. SSc ATA IgG are capable of inducting changes in macrophages having differential effects.

Macrophages ATA addition has been found to decrease CD206 and CD86 expression and enhance IL-10 and MerTK levels in both healthy controls and SSc patients, suggesting that ATA alone is able to induce cell quiescence. Different effects have been detected after cell stimulation by ATA:Topo-I immune complexes, that leads to no change in CD206, a significant increase of CD86 and reduction of IL-10 and less MerTK, consistent with M2b polarization. The addition of unfractioned SSc plasma, a known source of disease-related cytokines and growth factors, determines a complex activation of healthy control macrophages, as indicated by enhanced CD206, enhanced CD86 and greatly enhanced IL-10 and MerTK, with similar trends observed in SSc macrophages (except for the failure to induce IL-10). These results indicate a major influence of ATA on macrophage activation states, which are differentially induced dependent on presence of the Topoisomerase antigen. The formation of immune complexes with Topoisomerase released by damaged and apoptotic cells might have an important modulating effect on the induction of macrophages by ATA.

WNT signaling disruption in SSc skin fibrosis

Misplaced WNT expression driving fibrotic skin changes.

WNT signalling is differentially expressed between healthy controls and SSc patients.

Specifically, the expression of papillary/reticular marker genes in SSc skin shifts towards a reticular profile compared to controls. Investigating the expression of WNT3A target genes, an enrichment of WNT3A-regulated genes has been detected in papillary gene sets of healthy skin. The spatial distribution of β-catenin-positive fibroblasts in healthy skin, predominantly in the papillary dermis, contrasts with SSc skin, where a 2-fold increase is observed throughout the dermis. A gradient with enrichment of β-catenin-expressing fibroblasts in the papillary layer of healthy skin is no longer observed in SSc. Of note, an enrichment of WNT/β-catenin-signalling regulation genes has been found in the PI16+ population, which is mostly located in the reticular dermis in healthy skin, with no differences between the two layers in SSc skin. This study provides the first evidence of disrupted physiological WNT/β-catenin gradient in SSc, linked to the loss of papillary dermal structure.

Fibroblast diversity in SSc: thirteen subpopulations uncovered

New fibroblast clusters drive fibrosis in systemic sclerosis.

13 different subsets of fibroblasts have been identified in SSc skin. The frequencies of myofibroblast, $S1PR^{+}$, FAP^{high}, $Thy1^{+}ADAM^{high}PU.1^{high}$ and $ADAM12^{+}Gli1^{+}$ are significantly higher in SSc individuals compared to healthy controls (HC), while the levels of $PI16^{+}FAP^{+}$, $Thy1^{+}ADAM^{low}$ and $TFAM^{high}$ are significantly decreased in SSc.

Fibroblast populations are differentially distributed between HCs and SSc patients: in the subepithelial layer of the dermis, TFAMhigh subset is mainly expressed in healthy donors and ADAM12+Gli1+ in SSc patients. In the lower dermis, FAPhigh and Thy1+ADAM12+PU.1high fibroblasts are increased in SSc. Of interest, S1PR+ fibroblasts are expressed in both upper and lower dermis and their proportion is positively correlated with clinical parameters of fibrosis progression, including the mRSS.

Interferon and complement: a unique signature of SSc synovitis

Differentiating systemic sclerosis from rheumatoid arthritis through synovial gene expression.

A pauci-immune pathotype is characteristic of SSc synovitis, and neutrophils are more prevalent in RA as compared to SSc synovitis. Seven Synovial Fluid (SF) cell lines have been defined by the expression of marker genes *PRG4*, *CHI3L2*, *COMP*, *CXCL12*, *CXCL14*, *MFAP5*, and *POSTN*. The proportion of SF clusters differ between both diseases, with a higher enrichment of $MFAP5^{+}$ and $COMP^{+}$ SF in SSc, and $POSTN^{+}$ and $CXCL12^{+}$ SF in RA. 675 significant differentially expressed genes and several differentially actived signalling pathways have been identified between SSc and RA SF. In particular, SSc SF are enriched in IFN-α and IFN-γ and complement and coagulation pathways, especially in genes of the alternative complement pathway, suggesting a possible link between IFN and complement activity. RA SF show a strong enrichment in TNF-α signaling and inflammatory response genes. These findings lay the groundwork for the development of specific targeted therapies for synovitis in SSc.

GPR68 inhibition: a new frontier in SSc treatment

Targeting acid-sensing pathways to reduce fibrosis.

The efficacy of a GPR68 inhibitor (FT011) has been tested in SSc patients. GPR68 is an acid-sensing G protein-coupled receptor and a critical mediator of inflammation and fibrosis.

12-weeks of FT011 treatment led to a significant increase in the proportion of patients showing clinical improvement based on the Revised CRISS-25 (80%), compared to a 10% improvement in the Placebo group. Treatment with FT011 400mg led to a decrease in the fibrotic gene signature score, while in the Pacebo cohort the score increased from baseline at 12 weeks, implying that fibrosis and inflammatory signatures worsened in placebo and improved with FT011 treatment, based on the gene expression profile in skin. A dose dependent effect was observed, as a greater decrease in the fibrosis gene signature score was observed for the FT011 400 mg group compared to the FT011 200 mg group.

FT011 was safe and well tolerated, with no differences in drug-related adverse events between groups. This data support progression to late-stage clinical development for FT011 in SSc patients.

7. PRECISION MEDICINE AND NOVEL TARGET IN SYSTEMIC SCLEROSIS SESSION

By Stefano Di Donato

Commented by the main experts in the field, lectures and new works were presented in this session:

7.1 Right Time to Start Which Drug in SSc?

In systemic sclerosis (SSc), treatment timing is becoming increasingly guided by stratified and precision medicine approaches, much like the use of iberdomide in systemic lupus erythematosus trial based on interferon I signatures, which inform differing treatment responses.

As highlighted in the lecture from Professor Yannick Allanore, the timing of intervention is crucial, as it reflects the underlying immune processes driving disease progression. For instance, in SSc patients, bosentan has demonstrated improved ulcer outcomes when started within the first 5 years of disease duration. However, in pulmonary arterial hypertension (PAH), registry data showed no significant effect of disease duration on treatment response, yet other studies emphasize the benefits of early, upfront dual therapy, advocating a more aggressive and earlier approach in vascular management.

Regarding skin fibrosis, abatacept has been shown to be more effective in reducing the modified Rodnan skin score (mRSS) for those patients with a disease duration of less than 18 months, underscoring the importance of early treatment. Similarly, for interstitial lung disease (ILD), tocilizumab has been found to be more effective when started within 2 years of disease onset. By the same token, in a post-hoc analysis of the SENSCIS trial, nintedanib proved more effective in managing ILD in early disease. These findings emphasize the importance of early diagnosis and timely treatment to maximize therapeutic responses in SSc.

7.2 Individualised treatment of SSc

In the second lecture, Professor Oliver Distler discussed the updated ACR recommendations for the treatment of CTD-ILD. Notably, the guidelines introduced a new emphasis on treatment being "dependent on specific situation/patient factors," which has significant implications for clinicians. This flexibility is key, as it allows drugs like mycophenolate mofetil, tocilizumab, and rituximab to be considered equivalent first-line therapies in SSc, with nintedanib positioned as a second-line option alongside cyclophosphamide.

This approach marks a slight departure from the newer EULAR SSc-specific guidelines. However, a crucial challenge remains: the lack of data on differential responses between immunosuppressive and anti-fibrotic treatments, leaving uncertainty about how best to tailor therapy.

Professor Distler highlighted the need for a stratification factor, akin to Professor Pitzalis' work in rheumatoid arthritis, where synovial biopsy signatures are used to allocate treatment. This kind of personalized approach is still lacking in SSc, but it could greatly improve treatment outcomes. The presentation also featured clinical cases where patients were phenotyped based on trial inclusion criteria, showcasing different strategies for treatment allocation. These examples underscored the importance of addressing the multi-domain needs of SSc patients and the necessity for a more precise, data-driven approach to therapy in SSc-ILD.

7.3 Novel therapeutic targets in SSc

In her lecture, Professor Elizabeth Volkmann explored novel therapeutic targets in SSc, starting with a fundamental question: is fibrosis reversible? Drawing from research on the dynamic interplay of extracellular matrix deposition and degradation, she examined why this balance is disrupted in SSc and whether insights can be gained from COVID-19 cases, where incident fibrosis reversed in nearly half of patients by day 120.

Several key molecules that are currently under investigation were mentioned. LPAR1 (Lysophosphatidic Acid Receptor 1) antagonists, which inhibit this molecule expressed on macrophages and fibroblasts, are being studied for their effects on vascular constriction and neointimal proliferation. Additionally, cGC (soluble Guanylate Cyclase) inhibitors, known for promoting vasodilation, are being explored not just for their vascular effects but also for their potential to inhibit myofibroblast differentiation and influence the TGF-beta pathway.

In the realm of immune modulation, multiple CD20-targeting molecules are being developed to block B cell activity, a crucial player in SSc pathogenesis. The discussion then shifted to the current state of clinical trials, which largely focus on patients with early diffuse SSc and often have stringent inclusion criteria such as a modified Rodnan skin score>15, elevated CRP, or the presence of anti Scl-70 antibody. This, Professor Volkmann noted, leads to challenges with low generalizability and poor enrolment. She highlighted the need for innovative trial designs, such as basket trials, which allow for the inclusion of patients with different connective tissue diseases who share similar disease features.

Examples include the RECITAL trial, which compared rituximab and cyclophosphamide in ILD across multiple CTDs, and the EVER ILD trial, which accepted any type of ILD if it was characterized as nonspecific interstitial pneumonia (NSIP). Finally, Professor Volkmann emphasized the potential of synthetic control arms. These arms use real-world data or pooled data from previous trials to create comparison groups, reducing the need for placebo arms and accelerating patient recruitment. This approach could be a key strategy for speeding up the development of effective therapies in SSc.

7.4 CD19-Targeted CAR T Cells: a new alternative in stabilizing progressive systemic sclerosis

A first study presented preliminary results from an open-label, single-center pilot study evaluating the efficacy of CD19-targeting CAR T cell treatment in patients with dcSSc. Six patients with severe, progressive dcSSc, who had failed conventional therapies, were treated with CD19-targeting CAR T cells, with follow-up data collected over a one-year period. CD19 CAR T cells have previously shown success in treating refractory autoimmune diseases such as lupus erythematosus and inflammatory myopathy. The primary aim of this study was to assess the effects of deep B-cell depletion using CD19 CAR T cells on fibrotic skin disease progression, organ involvement, autoimmunity, and vascular phenomena.

All six patients (four males, two females) included in the study were experiencing dcSSc and were positive for either anti-Scl-70 (five) or anti-RNAP-III antibodies. The median age was 42 years, with a disease duration of approximately 36 months. The patients underwent lymphodepletion with fludarabine and cyclophosphamide before receiving a single infusion of CAR T cells. Following treatment, the modified Rodnan skin score (mRSS) decreased by 30-45% within the first 3-4 months and further improved by up to 60% over the course of the year. Raynaud's phenomenon also improved, and digital ulcerations became less frequent or completely absent.

Histological analysis of skin biopsies revealed a decrease in FAP-positive fibroblasts and a shift toward a more physiological papillary skin structure, with reduced collagen alignment and an increased number of papillae. Serological data showed significant decreases in ANA titers within three months, with continued declines over

the year. Anti-RNAP-III antibodies disappeared early after treatment and were undetectable throughout follow-up, while anti-Scl-70 antibodies persisted but with reduced titers. Lung function parameters remained stable in patients with interstitial lung disease (ILD), and imaging results using 68Ga-FAPI-04 demonstrated decreased fibrotic disease activity in the lungs and heart within three months, which remained stable throughout the year. The study provides promising evidence that CD19-targeting CAR T cell therapy can lead to disease stabilization in patients with severe dcSSc, with no need for additional immunosuppression during the one-year follow-up. The treatment also resulted in notable histological improvements in skin structure, suggesting a shift towards a healthier phenotype. Ongoing studies are expected to explore the underlying mechanisms of these effects.

GRK5: a key regulator of fibroblast activation and a novel therapeutic target in systemic sclerosis fibrosis.

A second study investigated the role of G protein-coupled receptor kinase 5 (GRK5) in the pathophysiology of fibrotic tissue remodelling in SSc. GRK5 is known for regulating G protein-coupled receptors by promoting their desensitization and internalization through phosphorylation. It has also been implicated in inflammation and tissue remodelling, though its role in fibrotic diseases such as SSc had not been explored before this study.
In this research, elevated levels of GRK5 mRNA and protein were observed in fibroblasts from fibrotic skin and lung tissues of SSc patients compared to non-fibrotic controls. This upregulation was also evident in murine models of SSc. The study further showed that TGFβ, a key mediator in fibrosis, induced GRK5 expression in fibroblasts. Knockdown of GRK5 reduced the fibroblasts' sensitivity to TGFβ, impairing the transition to myofibroblasts and decreasing collagen production. In vivo experiments demonstrated that GRK5 knockout in fibroblasts ameliorated fibrosis in models of both dermal and pulmonary fibrosis, whereas overexpression of GRK5 worsened fibrotic outcomes.
These findings suggest that GRK5 plays a pivotal role in the activation of fibroblasts in response to TGFβ, highlighting it as a potential therapeutic target for antifibrotic treatments SSc.

8. SYSTEMIC SCLEROSIS POSTER TOUR – SESSION II

By Stefano Di Donato

The following abstracts were provided were presented during the Clinical Poster Tour, Session I, at EULAR 2024. Topics range from gastrointestinal and pulmonary complications to the development of prognostic biomarkers, each offering a glimpse into the future of SSc management and therapy.

8.1 Sulli et al. - Aminaphtone short-term treatment reduces TGF-Beta plasma levels in systemic sclerosis patients with secondary raynaud's phenomenon.

The study investigates the short-term effects of aminaphtone, a vasoactive drug, on TGF-beta plasma levels in SSc patients with secondary Raynaud's phenomenon (RP). Aminaphtone has previously shown effectiveness in reducing RP symptoms and enhancing blood perfusion. In this study, 26 SSc patients with secondary RP received aminaphtone treatment (75 mg twice daily) for 12 weeks. Plasma TGF-beta levels were measured at baseline (W0), 3 weeks (W3), and 12 weeks (W12) using ELISA. A significant reduction in TGF-beta levels was observed at W12 compared to baseline, particularly in patients who responded better to the treatment as indicated by improved blood perfusion. The findings suggest that aminaphtone may decrease TGF-beta, a mediator of fibrosis, and serve as a useful adjunct therapy for RP in SSc.

8.2 Di Donato et al. MRI DAVIX index shows biological face validity: cytometry analysis of endothelial cells in systemic sclerosis patients.

This study explored the relationship between vascular damage and endothelial cell subpopulations in SSc patients, using the MRI Digital Artery Volume Index (DAVIX) and flow cytometry analysis of circulating endothelial cells (CECs). Sixty-eight SSc patients were included, with DAVIX and CEC subpopulations measured. Patients with active digital ulcers had higher numbers of mature/activated CECs and lower DAVIX scores, indicating more severe vascular damage. Significant correlations were found between DAVIX, CEC counts, capillaroscopy patterns, and disease severity, such as DLCO and mRSS. DAVIX was validated as a reliable biomarker for vascular involvement in SSc, showing promise as a tool for patient stratification and monitoring.

8.3 Di Donato et al. - Digital Artery Volume Index (DAVIX): a contrast-free MRI surrogate for digital ulcer disease activity in systemic sclerosis

DAVIX, a novel contrast-free MRI index, was investigated as a predictor of digital ulcer disease activity in SSc. The study aimed to establish its validity as a vascular outcome measure in SSc. In a cohort of 227 SSc patients, DAVIX was calculated and compared across groups with and without DU disease. Patients with DU disease had significantly lower DAVIX scores, which were strongly predictive of new ulcer development over a 12-month follow-up. DAVIX also correlated with DLCO, FVC/DLCO ratios, and

mRSS, demonstrating its utility as a non-invasive surrogate marker for vascular complications and digital ulcer activity in SSc.

8.4 Feng et al. - Temporal association between breast cancer and systemic sclerosis: a cross-sectional analysis.

The study explores the temporal relationship between breast cancer and SSc to determine whether patients are at increased risk of developing one disease after the other. In a cohort of 625 SSc patients, 32 cases of breast cancer were identified, representing 5.13% of the population. The study found that 50% of these patients were diagnosed with breast cancer within three years of SSc diagnosis. A higher risk of breast cancer was associated with non-MMF immunosuppressant use, while MMF was associated with reduced risk. These findings suggest a temporal association between breast cancer and SSc, warranting further investigation to optimize patient monitoring and treatment strategies.

8.5 Kakkar et al. - Subclinical loss of lung volumes in Very Early Systemic Sclerosis: evidence from the VEDOSS database.

The study aims to investigate subclinical lung volume loss in patients with very early systemic sclerosis (VEDOSS), based on data from the VEDOSS project. Among 378 VEDOSS patients with serial lung function tests, 17.2% showed subclinical loss of lung volumes, with an FVC decline of ≥10% and/or a DLCO decline of ≥15% over time. Approximately half of these subclinical progressors met ACR/EULAR criteria during follow-up, underscoring the importance of early lung function monitoring. The findings highlight a potential preclinical phase of SSc lung involvement and the need for proactive screening and intervention.

8.6 Muraru et al. - Drivers of disease burden in systemic sclerosis: insights from the EULAR ScleroID questionnaire.

This study examines the drivers of disease burden in SSc patients, using the EULAR ScleroID questionnaire to analyze patient-reported outcomes and disease impact across clinical and demographic subgroups. An analysis of 471 SSc patients revealed significant correlations between ScleroID scores and factors such as disease duration, digital ulcers, dyspnea, interstitial lung disease (ILD), and lower education levels. The ScleroID score correlated strongly with patient-reported disease activity but only weakly with physician-assessed disease activity. The study emphasizes the importance of integrating patient-reported outcomes into routine care for more comprehensive monitoring of disease burden in SSc.

8.7 Pedretti et al. - Disease subset and duration are associated with increased disease burden in systemic sclerosis: insights from the ScleroID questionnaire.

This study investigates the relationship between SSc disease subset, duration, and patient-reported disease burden using the ScleroID questionnaire in an Italian cohort. Data from 212 SSc patients revealed that disease duration and diffuse cutaneous involvement were independently associated with higher ScleroID scores, reflecting greater disease burden. Fatigue, Raynaud's phenomenon, and hand function were reported as the most impactful dimensions of disease. The findings suggest that disease subset and duration significantly influence the patient-perceived disease burden, supporting the need for tailored management approaches in SSc.

8.8 Joerns et al. - Interstitial pneumonia with autoimmune features (IPAF) is prevalent among lung transplant recipients.

Introduction: This study assesses the prevalence of interstitial pneumonia with autoimmune features (IPAF) among lung transplant recipients, emphasizing the risk of progressive pulmonary fibrosis (PPF) in these patients. Of 114 lung transplant recipients, 31% met criteria for IPAF. Most IPAF cases were unrecognized prior to transplant, with diagnosis confirmed through pathology of explanted lungs. The findings suggest that IPAF is an under-recognized cause of end-stage lung disease requiring transplantation, and clinicians should be vigilant in identifying autoimmune features in patients with interstitial lung disease to optimize treatment and outcomes.

8.9 Praastrup et al. - Healthcare utilization preceding systemic sclerosis diagnosis: a nationwide Danish registry study.

The study investigates healthcare utilization patterns in the three years preceding a SSc diagnosis to identify opportunities for earlier intervention. In this Danish registry study, 1,650 SSc patients were compared to matched controls. Patients with SSc showed significantly higher healthcare utilization, particularly in the two years leading up to diagnosis, with an increase in general practice visits, hospital contacts, and radiological examinations. The study highlights the potential for earlier diagnosis through more efficient healthcare referral processes, especially when patients present with early, nonspecific symptoms of SSc.