

**Objectives:** The objective of this study is to evaluate the impact of the COVID-19 pandemic on rheumatology patients in Northern Ireland by assessing demographics, rheumatic disease, medications, disease progress, shielding advice, access to primary & tertiary care and incidence of COVID-19 infection.

**Methods:** A web-based cross-sectional survey was completed in Northern Ireland. The study duration was between 23<sup>rd</sup> November 2020 and 22<sup>nd</sup> January 2021. The questionnaire included consent, demographic details, medication history, comorbidities, disease course, patient experience, shielding advice, COVID-19 illness and hospitalisation. The survey was publicised by sending 6,032 Belfast Trust NHS patients a link via SMS, posters were displayed in rheumatology departments, and links made available via NHS/Versus Arthritis social media platforms.

**Results:** There were 2,615 responses and of these 2,539 had been completed and were analysed. Most respondents were aged 45+ (78.27%) and female (N=1819). Rheumatoid arthritis (41%) and psoriatic arthritis (29%) were the most common diagnoses. Just over one third (35.27%, N=896) of patients were on biological drugs. Most patients were taking methotrexate (28.04%) followed by hydroxychloroquine (15.20%) and adalimumab (12.52%). The majority (79.6%) continued treatment during the pandemic. There was evidence of disease 'flaring' in 30.75% of patients who had stopped treatment. Of the respondents surveyed 7.8% (N=198), tested positive for Covid-19 and of these 77.55% reported that they had received adequate shielding advice, primarily from GP or UK government sources. Only 11.11% (N=22) of those who tested positive for Covid-19 required hospital admission and 2 patients required intensive care support. Both patients requiring ICU were not on immunosuppression. Less than one third of patients testing positive for COVID-19 were on biological drugs (30.3%, N=60). Cardiovascular disease was the most prevalent comorbidity. Of the 22 patients hospitalised with COVID-19, 13.64% (N=3) were on solitary sulphasalazine therapy.

**Conclusion:** The survey showed low levels of COVID-19 hospitalisation despite most patients continuing DMARD/biologic/glucocorticoid therapy. This has been replicated in other studies<sup>1</sup>, however data continues to be gathered on the safety of some biologic drugs particularly rituximab<sup>2</sup>. Most of our patients received clear understandable shielding guidance from a variety of sources. Many patients expressed fear of mortality, isolation and mental health issues. The survey findings indicated that stopping medication can have a negative impact on disease control.

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## Progress in myositis and scleroderma research - II

OP0266

### EFFICACY OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSc-ILD) AND INTERNAL ORGAN INVOLVEMENT: DATA FROM THE SENSICIS TRIAL

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**Background:** SSc is a heterogeneous autoimmune disease characterised by fibrosis of the skin and internal organs. In most patients with SSc-ILD, organs other than the lungs are also affected. In the SENSICIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% versus placebo.

**Objectives:** We investigated the extent of organ involvement related to SSc at baseline in patients in the SENSICIS trial and the effect of nintedanib versus placebo on the rate of FVC decline in subgroups by internal organ involvement.

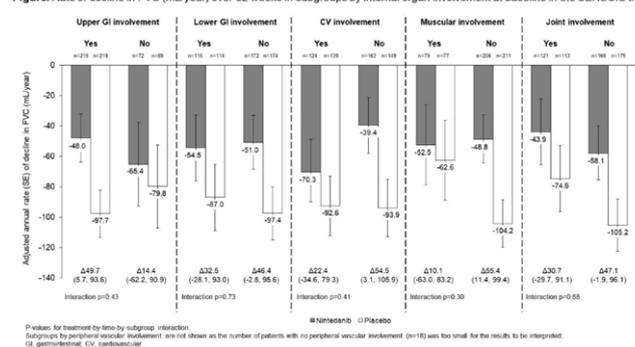
**Methods:** The SENSICIS trial enrolled patients with SSc-ILD with first non-Raynaud symptom  $\leq 7$  years before screening, extent of fibrotic ILD  $\geq 10\%$  on high-resolution computed tomography (HRCT) and FVC  $\geq 40\%$  predicted. Patients with clinically significant pulmonary hypertension were excluded. Patients were randomised to receive nintedanib or placebo until the last patient reached week 52

but for  $\leq 100$  weeks. In post-hoc analyses, we analysed the rate of decline in FVC (mL/year) over 52 weeks in subgroups with and without different types of SSc-related internal organ involvement (upper gastrointestinal; lower gastrointestinal; cardiovascular [CV]; peripheral vascular; muscular; joint). These subgroups were defined based on patients' SSc-related medical history as reported in the case report form. A random slope and intercept model was used to assess the rate of decline in FVC (mL/year) and an interaction test applied to assess potential heterogeneity in the treatment effect of nintedanib between the subgroups.

**Results:** Of 576 patients, 96.9% had peripheral vascular involvement, 75.5% had upper gastrointestinal and 39.8% lower gastrointestinal involvement, 45.7% had CV involvement, 40.6% had joint involvement, and 27.1% had muscular involvement at baseline. In the placebo group, the rate of decline in FVC (mL/year) was numerically greater in patients with than without upper gastrointestinal involvement and in patients without than with joint involvement or muscular involvement (Figure). The exploratory interaction p-values did not indicate heterogeneity in the treatment effect of nintedanib versus placebo on reducing the rate of decline in FVC (mL/year) between the subgroups based on organ involvement ( $p > 0.05$  for all treatment-by-time-by-subgroup interactions) (Figure).

**Conclusion:** Patients in the SENSICIS trial had diverse complications related to SSc. There was no evidence of a differential treatment effect of nintedanib on reducing the rate of decline in FVC based on gastrointestinal, CV, joint, or muscular involvement at baseline.

Figure. Rate of decline in FVC (mL/year) over 52 weeks in subgroups by internal organ involvement at baseline in the SENSICIS trial.



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OP0267

### SHORT-TERM CHANGES IN THE RADIOGRAPHIC EXTENT OF INTERSTITIAL LUNG DISEASE PREDICT LONG-TERM MORTALITY IN SYSTEMIC SCLEROSIS

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**Background:** The forced vital capacity (FVC) is often used as the primary endpoint in treatment trials for systemic sclerosis-interstitial lung disease (SSc-ILD), and while trends in FVC have been found to predict mortality in SSc-ILD,<sup>1,2</sup> FVC measurements are also influenced by extra-pulmonary factors, such as cutaneous sclerosis, myopathy, and patient/technician effort. Change in the quantitative extent of ILD (QILD) on HRCT is an emerging endpoint in clinical trials; however, no studies have evaluated whether changes in radiographic extent ILD predict mortality in SSc-ILD.

**Objectives:** To evaluate the relationship between changes QILD in the whole lung (WL) and long-term survival in patients who participated in the Scleroderma Lung Study (SLS) I<sup>3</sup> and II.<sup>4</sup>

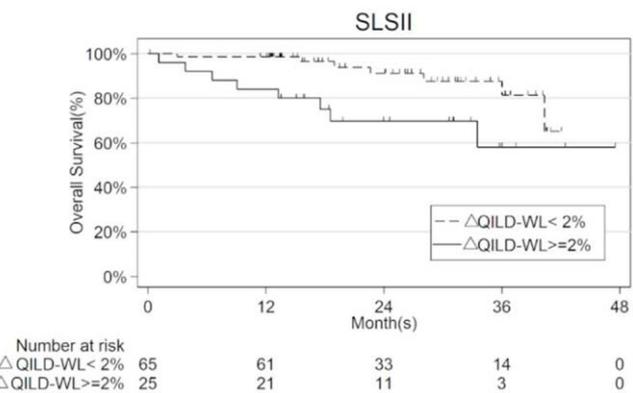
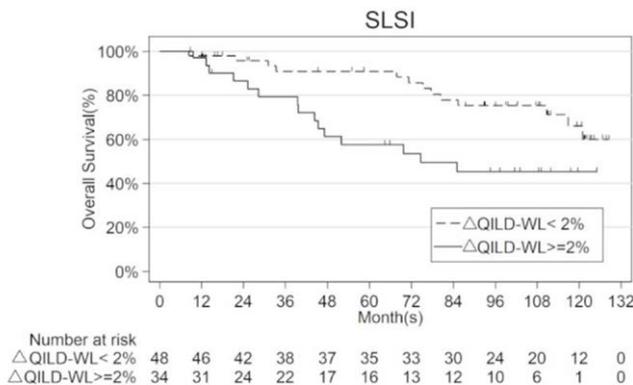
**Methods:** SLS I randomized 158 SSc-ILD patients to 12 months of cyclophosphamide (CYC) vs. placebo. SLS II randomized 142 SSc-ILD patients to 12 months of CYC, followed by 12 months of placebo vs. 24 months of mycophenolate (MMF). QILD-WL scores were calculated at baseline and 12 months (SLS I) and 24 months (SLS II). Participants were followed for up to 12 (SLS I) and 8 years (SLS II). Using landmark survival analysis, Kaplan Meier curves were generated to compare survival between participants who had worse QILD-WL scores ( $\geq 2\%$  increase) and those who had stable/improved QILD-WL scores ( $< 2\%$  increase). Cox proportional hazards models were created to determine whether the change in QILD-WL scores predicted survival after controlling other variables found to affect survival in these cohorts.

**Results:** Among all the SLS I and II participants, 82 and 90 had follow up HRCT scans, respectively, and were included in these analyses. SLS I participants with an increase in QILD-WL scores of  $\geq 2\%$  at 12 months had significantly worse long-term survival ( $P = 0.01$ ; Figure). Similarly, SLS II participants with an increase in QILD-WL scores of  $\geq 2\%$  at 24 months had significantly worse long-term survival ( $P = 0.019$ ; Figure). After adjusting for baseline FVC, age, and modified Rodnan skin score (mRSS), an increase in QILD-WL scores of  $\geq 2\%$  remained associated with worse long-term survival in SLS I (*trend*:  $P = 0.089$ ) and SLS II ( $P = 0.014$ ).

**Conclusion:** Progression of the radiographic extent of ILD of  $\geq 2\%$  was associated with worse long-term survival in two independent SSc cohorts with extensive long-term follow up. The findings provide compelling evidence that short-term changes in the radiographic extent of ILD may serve as a surrogate endpoint for mortality in patients with SSc.

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OP0268 **TREATMENT STATUS AFFECTS HOW PULMONARY BIOMARKERS PREDICT PROGRESSION OF SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE**

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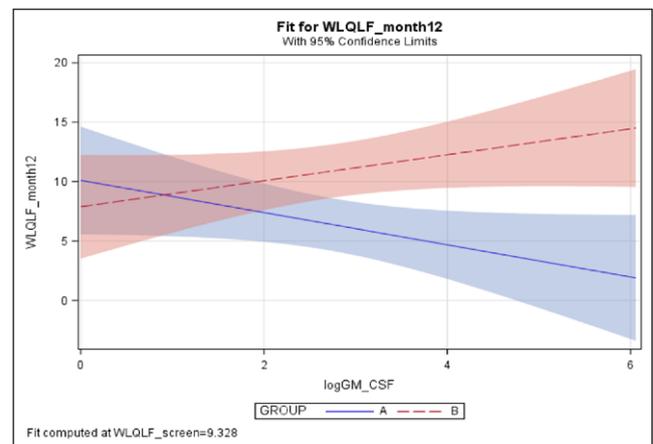
**Background:** The course of interstitial lung disease (ILD) varies considerably in patients with systemic sclerosis (SSc), and no biomarkers have been found to

consistently predict ILD progression in this population. Treatment may affect how a candidate biomarker correlates with improvement/worsening of SSc-ILD. We hypothesized that specific proteins recovered from bronchoalveolar lavage (BAL) would differentially predict progression of SSc-ILD based on whether a patient was receiving ILD therapy.

**Objectives:** (1) To assess the relationship between 68 unique BAL proteins measured in participants of Scleroderma Lung Study (SLS) I<sup>1</sup> and changes in radiographic extent of SSc-ILD; (2) To determine if treatment affects whether a specific protein predicts improvement or worsening of SSc-ILD.

**Methods:** Bronchoscopy was performed on 144 of the 158 participants in SLS I (Cyclophosphamide [CYC] vs. placebo) with 103 BAL samples available for analysis. BAL was lyophilized, concentrated 10X and used in a multiplex protein analysis of 68 distinct cytokines, chemokines and growth factors. Quantitative imaging analysis (QIA) was used to calculate the extent of radiographic fibrosis (QLF) in the whole lung using HRCT of the chest at baseline and 12 months. Multivariable linear regression models were created to determine the key BAL proteins associated with change in QLF scores using a backward selection process adjusting for treatment arm and ILD severity. The bootstrap procedure was employed for internal validation.

**Results:** A number of BAL proteins were significantly associated with change in QLF scores at 12 months; however, the directionality of these associations was often based on the presence/absence of treatment. For example, increased levels of granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin (IL)-1, monocyte chemoattractant protein (MCP)-3, chemokine ligand (CCL)-5, transforming growth factor (TGF)- $\beta$ , hepatocyte growth factor (HGF), stem cell factor (SCF), IL-4, TGF- $\alpha$ , were associated with worse QLF scores in patients who received placebo; whereas, increased levels of these same proteins were associated with improved QLF scores in patients who received CYC (Figure). Increased levels of Fractalkine were associated with worse in QLF scores, and increased levels of IL-7 were associated with improved QLF scores, regardless of treatment arm. In the multivariable model adjusting for treatment arm and baseline severity of ILD, IL-1, MCP-3, surfactant protein C, IL-7, and CCL-5 were independently associated with change in QLF scores.



**Figure 1.** Example of a specific BAL protein (GM-CSF) that predicts worse QLF scores in patients receiving placebo (Group B, Red dotted line) and improved QLF scores in patients receiving CYC (Group A, Blue solid line). Shaded areas represent 95% confidence intervals.

**Conclusion:** Proteins that mediate both inflammation and fibrosis differentially affected progression of SSc-ILD based on treatment status. Higher levels of certain proteins predicted worsening of ILD in patients receiving placebo, but improvement in patients receiving CYC. Measuring these proteins could help to identify patients who: (1) are at risk for ILD progression, and (2) may preferentially benefit from treatment with immunosuppression.

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OP0269 **A COMBINED CLINICAL AND BIOMARKER ALGORITHM TO PREDICT FVC DECLINE IN SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE: RESULTS FROM AN INTERNATIONAL MULTICENTRE OBSERVATIONAL COHORT**

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