EUSTAR Fellowship Report – Dr. Nicola Ortalli

Host Institution: Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), Leeds Teaching Hospitals NHS Trust – Scleroderma Unit, United Kingdom

Home Institution: Rheumatology Unit, AOU and University of Cagliari, Department of Medical Sciences and Public Health, Italy

Supervisor: Prof. Francesco Del Galdo

Fellowship period: 11/05/2025–31/07/2025

My name is Nicola Ortalli, a rheumatology resident from the University of Cagliari, Italy. I had the opportunity to carry out my EUSTAR Fellowship at the Scleroderma Unit in the Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), one of the most active centers in Europe for systemic sclerosis, under the guidance of Prof. Francesco Del Galdo. This experience was highly formative, both professionally and scientifically, and surely enhanced my knowledge of early systemic sclerosis and its pulmonary manifestations.

From the beginning, I was immersed in a multidisciplinary environment where systemic sclerosis is approached through structured, protocol-based care. The integration of clinical management and research was particularly striking, especially compared to more traditional models I was used to. I was able to observe how early organ involvement is systematically screened and how longitudinal data is actively used to inform clinical decisions.

The main focus of my project was on patients with Very Early Diagnosis of Systemic Sclerosis (VEDOSS), defined by the presence of Raynaud's phenomenon and at least one additional SSc-related feature (positive ANA, disease-specific autoantibodies, or abnormal capillaroscopy). The study aimed to detect early signs of interstitial lung disease (ILD) progression using established PF-ILD criteria, and to correlate these with circulating biomarkers and imaging features, particularly lung ultrasound.

I was involved in the processing of clinical data and in the creation of longitudinal variables such as ΔFVC% and ΔDLCO%. I also supported the analysis of molecular data, including biomarkers of fibrosis such as the Enhanced Liver Fibrosis (ELF) score (based on hyaluronic acid, TIMP-1, and PIIINP) and INF score.

Out of 82 VEDOSS patients included in the study, 17% showed pulmonary function decline over a median follow-up of 36 months, consistent with PF-ILD definitions. Notably, these patients already had lower DLCO values at baseline, suggesting impairment even before formal disease classification. Higher baseline levels of ELF and PC3P were associated with increased risk of progression (OR 2.66 and OR 1.32, respectively), while hyaluronic acid levels negatively correlated with both ΔFVC% and ΔDLCO%, reinforcing its potential as a dynamic marker of fibrotic activity.

Conversely, the interferon (IFN) chemokine score, despite being a recognized marker in SSc pathogenesis, did not show a significant difference between lung progressors and non-lung progressors.

These preliminary findings support the concept that lung involvement can occur early in the disease course and that certain biomarkers may help identify VEDOSS patients at higher risk. This could contribute to future strategies for early screening and targeted intervention.

A particularly innovative aspect of the project was the integration of lung ultrasound as a screening tool. At LIRMM in Leeds, lung ultrasound is increasingly used alongside pulmonary function testing for early detection of ILD. During the fellowship, I had the chance to observe the acquisition and interpretation of lung ultrasound exams. We began analyzing a subset of VEDOSS patients for B-line distribution and pleural abnormalities, which will later be correlated with functional decline and biomarker data. This part of the work is still ongoing, and lung ultrasound findings will be incorporated into the final analysis once fully processed. The longitudinal, multimodal nature of this dataset will allow for a more refined stratification of risk in early SSc.

Beyond the central research project, I actively took part in weekly SSc multidisciplinary team meetings and imaging sessions involving advanced techniques such as skin OCT and gastrointestinal ultrasound.

The environment at Leeds was academically vibrant and scientifically stimulating. I had the opportunity to interact with researchers and fellows from other centers, opening the door to future collaborations. Upon returning to Italy, I plan to continue working with the Leeds team remotely on data interpretation and paper preparation. Moreover, we are discussing the potential creation of a validation cohort at my home institution, and the implementation of early screening protocols including lung ultrasound.

In summary, this fellowship was a major step in my clinical and academic development. It enabled me to acquire technical and analytical skills, gain exposure to translational research models, and contribute to a meaningful project in early systemic sclerosis. Although some components of the study are still ongoing, the preliminary results are promising and form the basis for further work.

I am extremely grateful to EUSTAR for this unique opportunity, to Prof. Del Galdo and the Leeds team for their warm welcome and scientific guidance, and to Prof. Cauli, my supervisor in Cagliari, for his continuous support and commitment to advancing the care of patients with systemic sclerosis. I highly recommend this programme to other early-career clinicians and researchers interested in pursuing a path in SSc clinical care and research.

Sincerely,

Dr. Nicola Ortalli

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