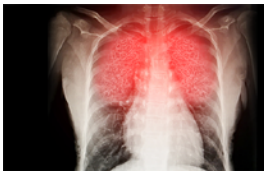


SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE:
MAKING CONNECTIONS, ELEVATING CARE

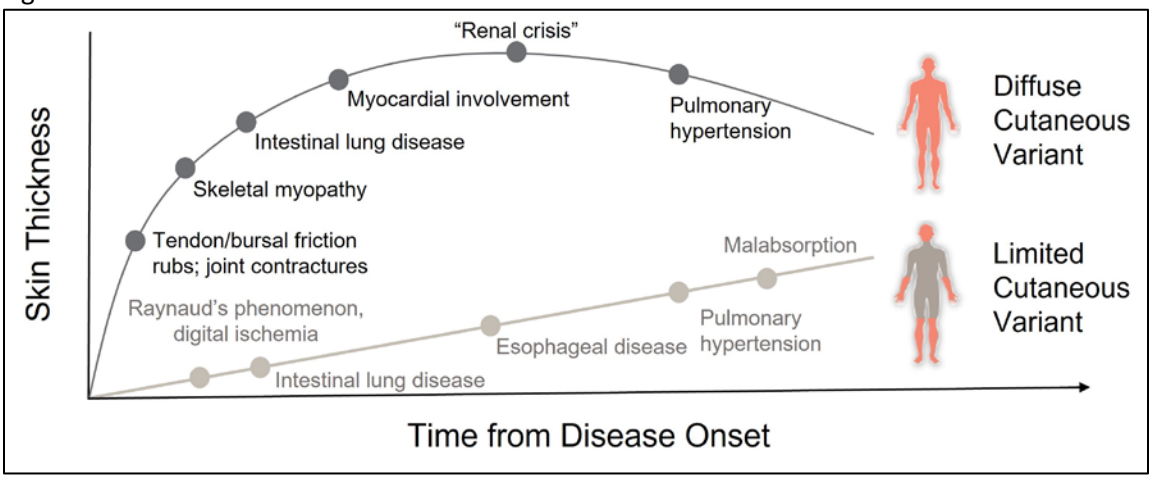
Prevalence, Patient Burden, Need for Screening

- Understanding the epidemiology is critical for this rare multisystemic connective tissue disorder. Interstitial lung disease (ILD) is very common in patients with systemic sclerosis (SSc), also known as scleroderma, with some level of significant ILD occurring in 30% to 40%. ILD may occur in patients with SSc without skin involvement. The 10-year mortality rate may be as high as 40%.
- The onset of ILD is often within 4 to 5 years of the initial symptom of SSc and is often asymptomatic. Therefore, screening patients for lung involvement is particularly important within the first few years of SSc diagnosis.
- The prevalence of ILD is 96% in those with SSc who have an abnormal pulmonary function test (PFT).
- High-resolution computed tomography (HRCT) is the most sensitive screening tool available to identify underlying ILD, supplanting lung biopsy for diagnosis. Interstitial abnormalities become evident on an HRCT scan of the chest in 80% of patients with SSc. The HRCT scan provides a clear image of underlying lung function, including potential for ground-glass opacity. Prone, supine, inspiratory, and expiratory images should be obtained to review the dynamics of the lung and any change in shift. HRCT should be used along with the PFTs. The PFTs are helpful to provide longitudinal declines and, if observed, to what extent and at what level ILD may be progressing.
- The patient burden of disease is variable, thereby complicating the diagnosis and the treatment plan.

Risk Factors and Comorbidities

- SSc typically follows 1 of 2 disease courses: limited cutaneous variant or diffuse cutaneous variant (Figure 1).

Figure 1: SSc Disease Course

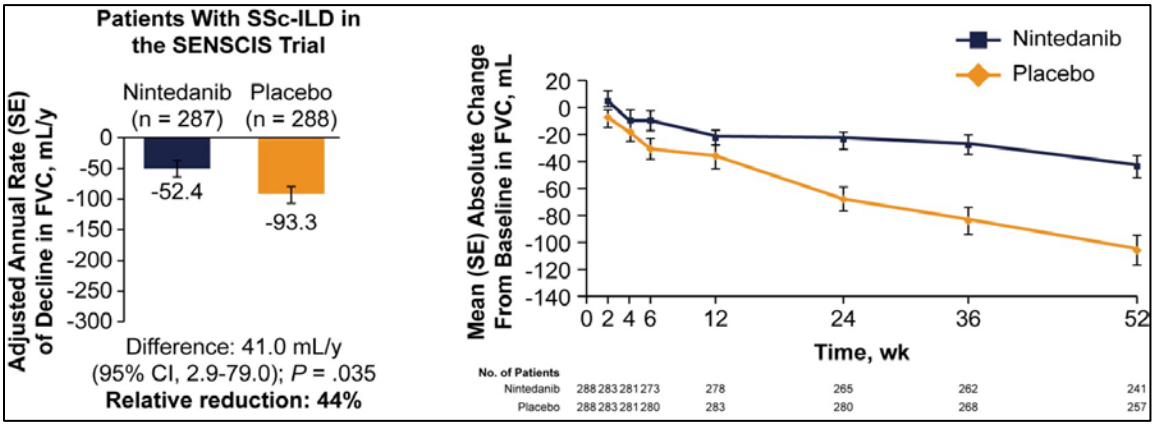


- Several factors are associated with progressive SSc-ILD, including African American race, male sex, advanced age, diffuse cutaneous disease, and greater lung involvement at diagnosis.
- Beyond the skin and lungs, a wide variety of organs and tissues may be involved in patients with SSc, including the gastrointestinal tract, heart, kidneys, and musculoskeletal system. Vascular damage and extensive fibrosis contribute to irreversible organ damage. Raynaud's phenomenon is common, as are autoimmune diseases such as rheumatoid arthritis and myositis. Multidisciplinary care is essential.

Current and Emerging Therapy

- The advent of pharmacologic options beyond immunosuppressives that are effective in slowing disease progression provides an opportunity for early intervention in patients with SSc-ILD, particularly those early in the disease course or with aggressive disease. Traditional therapy with immunosuppressive therapy yields some short-term benefit, but long-term benefit is limited. Moreover, treatment toxicity often limits use.
- Nintedanib and tocilizumab have recently been approved by the US Food and Drug Administration for the treatment of patients with SSc-ILD.
- Nintedanib is an oral targeted tyrosine kinase inhibitor that is considered as first-line therapy for patients with a predominantly fibrotic pattern on their HRCT scan. The SENSCIS trial demonstrated a significantly reduced annual rate of decline in the forced vital capacity (FVC) with nintedanib compared with placebo (Figure 2), irrespective of treatment with mycophenolate mofetil at baseline. GI adverse events were more common in the nintedanib group.

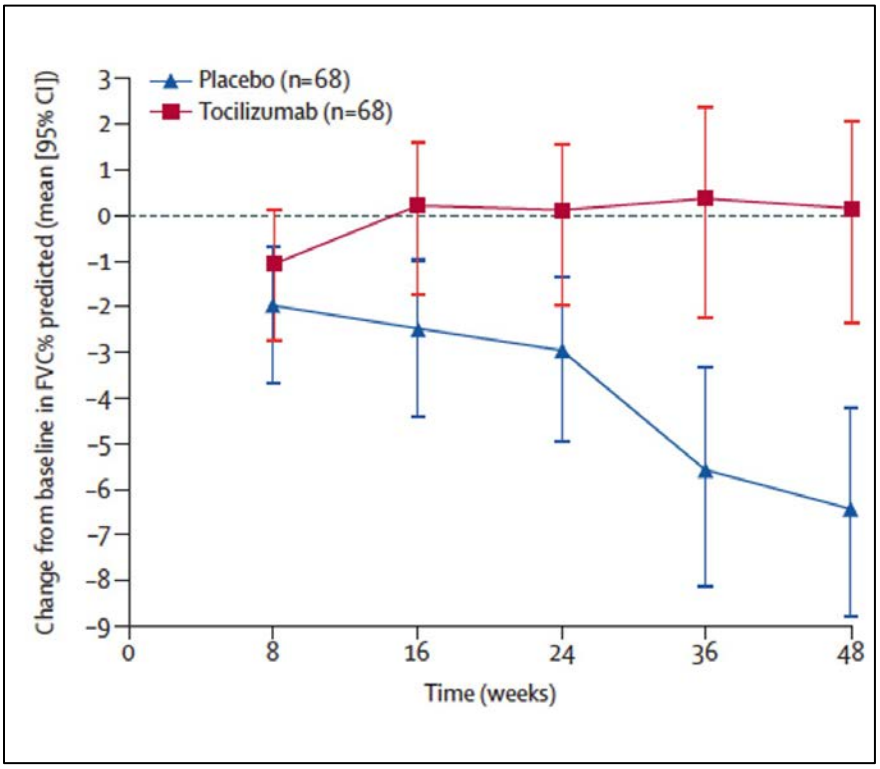
Figure2: Senscis: Results



FVC, forced vital capacity

- Tocilizumab is an anti-interleukin-6 receptor antibody. A phase 3 investigation of tocilizumab showed that the primary skin fibrosis endpoint was not met. However, tocilizumab preserved lung function in patients with early SSc-ILD and elevated acute-phase reactants (Figure 3).

Figure 3: Tocilizumab: Change from baseline FVC compared with placebo in patients dcSSc and ILD



dcSSc, diffuse cutaneous systemic sclerosis; FVC, forced vital capacity.

- Rituximab is used investigationally as a second-line agent, often in patients who experience progressive lung disease despite treatment with mycophenolate. Evidence for rituximab for SSc-ILD is limited, although it is being compared with cyclophosphamide in a phase 3 trial in patients with connective tissue disease-ILD.
- Pirfenidone, an anti-inflammatory and antifibrotic approved for the treatment of patients with interstitial pulmonary fibrosis, is being compared with mycophenolate in patients with SSc-ILD.