# Riociguat in systemic sclerosis: a potential for disease modification

We read with great interest the results of the recently published Riociguat Safety and Efficacy in Systemic Sclerosis (RISE-SSc) trial[1] and believe that additional analyses could further elucidate the role of riociguat in systemic sclerosis (SSc).

First, considering the pleiotropic (antifibrotic, anti-inflammatory and antiproliferative) actions of riociguat, an analysis of the radiographic findings [pattern- cellular non-specific interstitial pneumonia (NSIP), fibrotic NSIP or usual interstitial pneumonia (UIP); and the extent of fibrosis) in the subset of patients with interstitial lung disease (ILD) could provide useful preliminary information regarding the subset of SSc-ILD most likely be benefited with riociguat and the dominant mechanism behind its potential efficacy.

Second, what was the change in forced vital capacity (FVC) in millilitre in the two groups? As done in the Safety and Efficacy of Nintedanib in Systemic Sclerosis (SENSCIS) trial in SSc-ILD, studying absolute change in millilitre, rather than percentage predicted FVC, could help avoid masking early signals of efficacy.[2]

Third, a post hoc analysis of the effect of riociguat on swollen joints (31.4% patients), tender joints (42.1% patients), tenosynovitis and serum levels of C reactive protein could provide valuable evidence regarding the contribution of anti-inflammatory action[3] to its overall efficacy.

With an already proven efficacy in SSc-pulmonary hypertension[4] and early signals of efficacy in skin tightening, ILD and prevention of digital ulceration, riociguat holds promise as a potential disease-modifying agent in the diverse manifestations of SSc. Trials in SSc-ILD, and those employing the exploratory and post hoc endpoints of RISE-SSc as primary outcomes, are much needed.

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