Response to: 'Effectiveness and safety of tocilizumab for the treatment of refractory systemic sclerosis associated interstitial lung disease: a case series' by Narváez

We read the intriguing findings by Narváez[1] about the effect of tocilizumab (TCZ) in patients with established systemic sclerosis-associated interstitial lung disease (SSc-ILD) with great interest. In the double-blind, randomised, placebo-controlled faSScinate study[2] and open-label extension,[3] we assessed the efficacy and safety of TCZ in patients with systemic sclerosis. There were important differences between our trial and the data presented by Narváez[1]. In the faSScinate study, the patient population shown to benefit from TCZ had shorter duration of disease (mean disease duration of 1.6 years in faSScinate vs 6.9 years in Narváez), increased serum acute phase reactants, progressive skin disease and low normal mean forced vital capacity (FVC) levels (mean FVC% predicted of 81%) at study baseline. Compared with patients receiving placebo, patients receiving TCZ appeared to stabilise their FVC, an exploratory endpoint, and thus preserved their lung function: the mean change from baseline for FVC% predicted for placebo was −6.3% (95% CI −8.9 to 3.8) and for TCZ was −2.6% (−5.2 to −0.1) at week 48, with a delta of 3.7% (0.1 to 7.3); the delta in absolute millilitres for FVC at week 48 was 120 mL (−23 mL, 262 mL). These data are consistent with the findings from De Lauretis *et al*,[4] in which serum interleukin-6 levels appeared to be predictive of disease progression and/or death in patients with mild ILD (defined as FVC% >70%). The effect of TCZ on the lung has been speculated to be related to modulating the activity of M2 macrophages.[2] In contrast, Narváez[1] is studying TCZ as a rescue treatment in patients with SSc with established ILD who have failed rituximab (RTX) in all cases and cyclophosphamide in 67% of cases. All patients were on ongoing mycophenolate mofetil while receiving TCZ, with follow-up after first TCZ dose ranging from 6 to 34 months. TCZ may have contributed to the stabilisation of lung function in a more severe and resistant ILD, which is notable given patients' previous immunotherapy failures. It is interesting to note that all four patients who appeared to have responded to TCZ had pretreatment FVC% predicted of greater than 77% (mean FVC% was 84.8%). For patient 6, whose pretreatment FVC% was 108%, it is unclear if the decline in diffusing capacity for carbon monoxide (DLCO)% predicted represents worsening ILD or concomitant pulmonary vascular disease, especially with normal FVC% predicted (with no change over time) and an FVC to DLCO ratio of 1.56, a risk factor for pulmonary vascular disease in SSc.[5] Given these captivating case reports, controlled studies should be conducted to assess if indeed TCZ is having an effect in patients with severe established SSc lung disease.

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