rituximab as rescue therapy in interstitial lung disease refractory to conventional immunosuppression

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Background Rituximab, a B cell-depleting monoclonal antibody, may offer an effective rescue therapy in a subgroup of patients with severe interstitial lung disease (ILD), progressing despite conventional immunosuppressive treatment.

Methods Retrospective assessment of 50 patients with severe, progressive ILD treated with rituximab between 2010 and 2012. This included 33 with connective tissue disease-associated ILD (CTD-ILD), 6 with fibrotic hypersensitivity pneumonitis, 3 with likely drug-induced ILD, 2 with desquamative interstitial pneumonitis (DIP) and the rest with miscellaneous ILD patterns, excluding idiopathic pulmonary fibrosis. At the time of rituximab treatment, mean FVC was 49.1% (± 17.6) and DLco 25.5% (± 9.9). Four patients were mechanically ventilated. Prior to rituximab, all patients except one had received immunosuppressive treatment, including IV cyclophosphamide in 44 patients. Change in pulmonary function tests, as compared to pre-rituximab levels, was assessed at six to twelve months post-treatment and analysed by Wilcoxon signed rank test. Categorical trends (improvement, stability, deterioration) before and after treatment were defined using either ≥10% change in forced vital capacity (FVC) or ≥15% change in diffusing capacity for carbon monoxide (DLco) as threshold values.

Results In the six to twelve months following rituximab treatment, a median improvement in FVC of 5.7% (p < 0.01) and DLco (p < 0.01) was observed. This was in contrast to a median decline in FVC and DLco of 14.6% and 18.8% respectively, in the six to twelve months prior to rituximab therapy (p < 0.01). Patients with CTD-ILD were most represented in this cohort and were more likely to improve or stabilise following rituximab (28/33), than those with non CTD-related ILD (8/17) (p = 0.008, Fisher exact test). However, of the four patients requiring invasive ventilation, improvement to extubation was observed in three patients with non CTD-ILD (one DIP, one acute interstitial pneumonia, one unclassifiable ILD). Two patients developed serious infections (pneumonia) requiring hospitalisation following rituximab, and ten patients died, all from progression of underlying ILD, a median of 5.1 months after treatment.

Conclusions Rituximab may offer a safe and effective therapeutic intervention in a subgroup of patients with severe, progressive ILD unresponsive to conventional immunosuppression. Future prospective, controlled trials are warranted to validate these findings.