Appendix: Summary of relevant stu` dies identified

Reference	Study details	Main results
Systematic reviews		
CTD-ILD		
Zhang et al., 2025	A systematic review and meta-analysis of the efficacy of RTX to treat CTD-ILD. 40 studies included, involving 1052 patients. 14 studies reported the administration method of RTX as 1,000 mg administered twice with a two-week interval (p = 0.25), two studies administered 375 mg/m^2 once a week, a total of four times (p = 0.06), 21 studies did not report dosing information (p < 0.01). Changes in FVC% (40 studies) and DLCO% (36 studies) before and after RTX use were compared and analysed between RTX and control groups.	RTX significantly improved FVC% (WMD = 7.1, 95% CI = 4.58 to 9.62; p < 0.05) and DLCO% (WMD = 5.26, 95% CI= 2.86 to 7.65; p < 0.01), and reduced the mRSS (WMD = −6.58, 95% CI = −8.27 to −4.89; p < 0.01) and prednisone dose (WMD = −6.94, 95% CI = −11.96 to −1.92; p < 0.01). Among RTX-treated patients: 30.3% improved (25 studies; 95% CI = 22.0% to 39.3%); 45.3% remained stable (23 studies; 95% CI = 35.1% to 55.6%) and 10% progressed (26 studies; 95% CI = 5.7% to 15.1%). Pooled mortality from 30 studies was 5% (95% CI = 2.3% to 8.4%). The pooled hospitalisation rate from 16 studies was 6.7% (95% CI = 1.4% to 14.3%), and data from 16 studies showed a pooled infection rate of 22.4% (95% CI = 13.4% to 32.7%).
SSc-ILD		
Anwar et al., 2025	A meta-analysis and network meta-analysis of the effectiveness of CYC to treat SSc-ILD compared with placebo and other immunosuppressants including RTX. Eight studies included (four RCTs and four observational studies) involving 484 patients.	A mild but statistically insignificant difference was observed in FVC between CYC and RTX, yet the analysis leaned toward favouring CYC (overall [Cohen's d standard, −0.31; standard error, 0.19; 95% CI = −0.68 to 0.05; p = 0.09]). Network meta-analysis showed RTX had the lowest FVC outcome p score (0.3410), indicating a lesser

Reference	Study details	Main results
	57 patients (in 2 studies) were treated with two doses of IV RTX two weeks apart (doses ranged from 500–1000 mg). The review evaluated a range of lung function parameters. The difference in FVC between the CYC and RTX groups was reported.	impact on FVC outcomes compared to other treatments. However, variation in the CIs and weights for the fixed effects model versus the random effects model showed potential heterogeneity between the studies (I^2 = 0.81) and suggests that the meta-analysis was not robust. The study concluded that the findings do not decisively support the superiority of CYC over other treatments for most SSc-ILD lung function parameters.
Wu et al., 2025	A systematic review and meta-analysis evaluating the clinical effectiveness and safety of six treatments for SSc-ILD, including RTX. Eight randomised controlled trials, involving 1195 patients, were included. Two studies evaluating RTX were included; one at a dose of 375 mg/m^2 per week for four weeks (IV); one at a dose of 1,000 mg on Day 0 and Day 15 (IV). Outcomes included FVC% predicted, DLCO% predicted, and serious adverse events.	The study reported no significant statistical differences in efficacy and safety between the six treatments. However, in slowing the deterioration of FVC, TCZ (0.904) and RTX (0.709) ranked the highest in SUCRA (i.e. better-performing relative to other evaluated treatments). In improving DLCO, RTX (0.842) and MMF (0.566) ranked the highest. RTX showed the lowest probability for SAEs with a SUCRA ranking of 0.591. One patient died of severe pulmonary hypertension after 5 months of RTX treatment, which may be related to the disease process. One patient developed severe hypoalbuminemia, which led to the discontinuation of treatment. The study concluded that RTX and TCZ may be the optimal interventions for SSc-ILD.
ASS-ILD		

Reference	Study details	Main results
Kouranloo et al., 2025	A systematic review of the management and treatment outcomes for ASS-ILD. Ten studies were included (nine cohort studies and one case series) involving 514 patients. 88 patients received RTX (two infusions of 1 g of RTX on Day 1 and Day 15, or a dose of 375 mg/m^2 once weekly for four weeks). The review evaluated PFTs including FVC and DLCO. Where possible, meta-analysis using a random effects model was conducted for outcomes of PFTs.	Due to heterogeneity of methodology and cohorts, direct comparison was not possible for most drugs. Patients receiving RTX had an overall mean 12.2% improvement in FVC from baseline and a 2.9% increase in DLCO at one year. The review reported that two patients who receiving RTX died post-treatment due to *Pneumocystis jirovecii* infection. The review concluded that no conclusive difference between effectiveness of treatments was identified.
RA-ILD		
Ines et al., 2025	A systematic review and meta-analysis to study the efficacy and safety of RTX to treat RA-ILD. 20 studies were included, involving 1,619 patients who were given RTX. RTX dosage data were available in nine of the 20 studies; all these studies used the same regimen: RTX infusion of 1 g of RTX given on Day 1 and Day 15. Five studies reported that RTX infusions were preceded by pre-medication with 100 mg of methylprednisolone. PFTs were the most used evaluation method, followed by HRCT. Two studies reported survival and mortality rates.	Stabilisation or improvement of lung function was seen in more than half of the patient cohorts across all studies (42% to 100% based on PFTs; 42% to 87.5% by HRCT). All included studies concluded that RTX was effective in the management of RA-ILD, reducing the risk of progression. Meta-analysis results showed that the proportion of patients showing disease progression was 14.5% (95% CI=7.6% to 25.8%) (95% PI = 2% to 69%) based on PFTs; and 19.5% (95% CI = 8.1 to 40%) (95% PI = 1 to 84%) based on HRCT. An overall acceptable safety profile was noted, with respiratory-related mortality ranging from 4% to 14%. The most frequent adverse events were infections, with hospitalisation rates reaching approximately 21%.

Reference	Study details	Main results
Fassio et al., 2025	A systematic review and meta-analysis of studies evaluating pharmacological interventions for RA-ILD. 69 studies were included, involving 7879 patients. A total of 16 studies evaluating RTX in patients with RA-ILD were included. The review evaluated PFTs including differences in %FVC and %DLCO, risk of RA-ILD progression, severe adverse events, and mortality.	Pooled pre-post %FVC estimates were associated with stabilisation or improvement for most drugs, including RTX. Meta-analyses for RTX showed no significant differences in %DLCO changes compared to non-users of RTX. For RTX, a sensitivity analysis showed that, while the direction of the effect for %DLCO remained consistently positive across all iterations, statistical significance was observed when two studies were excluded, suggesting limited robustness of the pooled effect. Between study heterogeneity was high in all scenarios. The study concluded that ABA, RTX, and nintedanib appear to be promising treatment options for RA-ILD.
Clinical studies and retrospective studies		
SSc-ILD		
Barde et al., 2025	A French retrospective study of the efficacy and safety of MMF + RTX combination therapy compared with each drug given alone to treat SSc-ILD. Patients were treated with MMF + RTX, RTX or MMF or ≥12 months. 47 patients received MMF + RTX, 30 patients received only RTX and 50 patients received only MMF. 81% of all patients and 67% of the RTX only group had ILD involvement.	Results showed mRSS remained unchanged in the RTX group (8 [2–17] at baseline, to 8 [2–15] at 12 months, p = 0.3). FVC increased significantly only in the group that received RTX + MMF. Results from 23 patients in the RTX alone group showed increased FVC at 12 months but the change was not significant (64.5 [54.5–75.5] at baseline, to 68.0 [53.0–77.0] at 12 months; p = 0.8). After excluding cross-over patients, adverse events were more frequent in the combination group (n = 12; 44.4%) than in the RTX alone group (n = 4;

Reference	Study details	Main results
	Primary outcomes were changes in mRSS and predicted FVC from baseline to 12 months. In the RTX only group, RTX was given as two 1,000 mg doses 15 days apart for 27 patients, and as 375 mg/m^2 weekly for four weeks in three patients. 21 patients and 20 patients had a maintenance RTX dose at 6 and 12 months, respectively. All patients received premedication with methylprednisolone before RTX infusion.	22.2%) or MMF group (n = 6; 28.6%), including infections (n = 10, 37% versus n = 1, 5.6%, and n = 6, 28.6%). However, the differences were not statistically significant.
Yan et al., 2025	Data from a large European Scleroderma Trials and Research (EUSTAR) registry were used to compare the effectiveness of four treatments for SSc-ILD. Data analysed were from 955 patients from 103 centres and 997 treatment observations, and included 172 patients (17.3%) in the RTX group, 96 patients (9.6%) for TCZ, 511 (51.3%) for MMF, and 218 (21.9%) for CYC. The primary endpoint was the change in FVC percentage predicted from baseline to the follow-up visit closest to one year.	The median follow-up time was 11 months (IQR: 8-14 months). After inverse probability of treatment weighting (IPTW) the mean adjusted change in FVC percentage predicted from baseline to follow-up was not significantly different by multiple group comparison (p = 0.101). Paired comparisons showed no significant difference. It was concluded that TCZ, RTX, MMF and CYC showed comparable effectiveness in treating SSc-ILD. In some subanalyses, CYC showed clinically marginal but statistically significantly better effectiveness, mainly versus TCZ.

ABA: abatacept; ASS-ILD: anti-synthetase syndrome-associated interstitial lung disease; CI: confidence interval; CTD: connective tissue disease; CTD-ILD: connective tissue disease-associated interstitial lung disease; CYC: cyclophosphamide; DLCO: diffusing capacity of the lungs for carbon monoxide; FVC: forced vital capacity; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; IQR: interquartile range; IV: intravenous; MMF: mycophenolate mofetil; mRSS: modified Rodnan skin score; PFT: pulmonary function test; PI: prediction interval; RA-ILD: rheumatoid arthritis-associated interstitial lung disease; RCT: randomised controlled trial; RTX: rituximab; SAE: severe adverse events; SSc-ILD: systemic sclerosis-associated interstitial lung disease; SUCRA: surface under the cumulative ranking probability; TCZ: tocilizumab; WMD: weighted mean difference