SUPPLEMENTARY MATERIAL

METHODS:

The observation period was defined by the time from the first to the last RTX infusion. ILD was identified based on high-resolution CT. The results of forced vital capacity (FVC) and carbon monoxide diffusion capacity (DLCO) were collected at the time of the first RTX infusion, at month 12 and at the time of the last RTX infusion. BC immunophenotyping was performed the day of each RTX infusion (Aquios, Beckman Coulter). BC depletion was defined by CD19 <18/μL (1,2). CD19 counts had to be <18/μL at each infusion to consider the patient as having sustained BC depletion. Any FVC improvement was defined by any FVC increase from baseline to 12 months and from baseline to the last RTX infusion, excluding patients with FVC stabilization or decline.

All data are presented as median values with 95% confidence interval, CI or number and percentage (%) for continuous and categorical variables. Statistical analysis was performed using GraphPad Prism (v9.1.2). For a two-group comparison, Mann Whitney test was used (continuous variables). FVC values were compared between inclusion visit and month 12 or at the last RTX infusion using the Wilcoxon matched-pairs signed rank test.

Patient and Public Involvement statement: patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS:

In the subset of patients with sustained complete BC depletion, median FVC (%) increased from 84% (95% CI 51-116%) to 94% (95% CI 51-136%) at 12 months (p=0.034), then to 96% (95% CI 69-122%) at the last RTX infusion (p=0.021) (**Figure S1**). Conversely, in the subset of patients with incomplete BC depletion, FVC initially increased from 77% (95% CI 55-98%)

to 80% (95% CI 57-102%) at 12 months (p=0.7), before decreasing to 75% (95% CI 55-96%) at the last RTX infusion (p=0.73) (**Figure S1**).

DLCO was evaluated in 13 patients (The measure was not possible in 4 patients). In the subset of patients with sustained complete BC depletion, median DLCO initially increased from 4.95 L (n=7, 95% CI 3-13.35 L) to 5.13 L (n=7, 95% CI 2.92-14.22 L) at 12 months (p=0.58) before decreasing to 4.90 L (n=7, 95% CI 3.07-16.67 L) at the last RTX infusion (p=0.81). In the subset of patients with sustained incomplete BC depletion, DLCO initially increased from 3.83 L (n=6, 95% CI 2.78-14.64 L) to 4.18 L (n=6, 95% CI 3.33-10.22 L) at 12 months (p=0.84) before decreasing to 4.01 L (n=6, 95% CI 2.54-5.54 L) (p=0.69).

Bibliography

1. Avouac J, Cougnaud Murail R, Goulvestre C, et al. Immunogenicity of Rituximab biosimilar GP2013 in chronic inflammatory rheumatic disorders in daily clinical practice. Semin Arthritis Rheum. 2022 Feb;52:151951.
2. Avouac J, Miceli-Richard C, Combier A, et al. Risk factors of impaired humoral response to COVID-19 vaccination in rituximab-treated patients. Rheumatology. 2022 Jun 28;61(SI2):SI163–8.

Figure S1: Course of FVC (%) during the observation period according to B cell depletion; *p<0.05 vs baseline value by the Wilcoxon matched pairs signed rank test.

Table S1: Disease characteristics

	Patients with complete B cell depletion (n=9)	**Patients with incomplete B cell depletion (n=8)**
Age, median (95% CI)	59 (47-66)	58 (38-65)
Females, n (%)	7 (78)	7 (88)
Underlying disease		
SSc, n (%)	7 (78)	5 (62)
MCTD, n (%)	2 (22)	3 (38)
Disease duration, years median (95% CI)	9 (5-11)	7 (2-19)
Diffuse cutaneous SSc, n (%)	5/7 (71)	5/5 (100)
mRSS, median (IQR)	11 (24)	13 (11)
Antibody profile		
Positive antinuclear antibodies, n (%)	9 (100)	8 (100)
Positive antitopoisomérase antibodies, n (%)	5 (56)	3 (38)
Anti-RNP antibodies, n (%)	2 (22)	3 (38)
ILD pattern on chest HRCT		
NSIP, n (%)	3 (33)	3 (38)
SSc, n (%)	2 (67)	2 (67)
MCTD, n (%)	1 (33)	1 (33)
UIP, n (%)	6 (67)	5 (62)
SSc, n (%)	4 (67)	3 (60)
MCTD, n (%)	2 (33)	2 (40)
Baseline functional lung parameters		
FVC (L), median (95% CI)	2.58 (1.13-4.26)	2.05 (0.99-3.24)
FVC (%), median (95% CI)	84 (51-116)	77 (55-98)
DLCO (L), median (95% CI)	4.95 (3.00-13.35)	3.83 (2.78-14.64)
DLCO (%), median (95% CI)	72 (26-89)	75 (48-100)
Ongoing treatment		
Low dose corticosteroids, n (%)	5 (56)	2 (25)
Methotrexate, n (%)	3 (33)	4 (40)
Mycophenolate mofetil, n (%)	3 (33)	2 (25)
Other, n (%)	2 (22)	1 (13)

SSc: Systemic Sclerosis, MCTD: Mixed Connective Tissue Disease, NSIP: Non-Specific Interstitial Pneumonia, UIP: Usual Interstitial Pneumonia, FVC: Forced Vital Capacity, DLCO: Carbon Monoxide Diffusion capacity

Table S2: Treatment with Rituximab according to B cell depletion during the observation period

	Patients with complete B cell depletion (n=9)	Patients with incomplete B cell depletion (n=8)
Duration of RTX exposure (months) median (95% CI)	48 (18-107)	36 (18-97)
Number of infusions, median (95% CI)	9 (4-15)	6 (3-17)
Cumulative dose (g), median, (95% CI)	7 (4-11)	5 (1.5-15)
RTX Dose (g) / infusion, median, (95% CI)	1 (0.5-1)	1 (0.5-1)
CD19 (/mL), median (95% CI)	15 (13-18)	70 (18-126)
CD19 ≤18/ µL	9 (100)	0 (0)