Supplementary Table S1. Definitions of organ involvement.

	Criteria for diagnosis
Pulmonary fibrosis	Basal fibrosis on high resolution computed tomography (HRCT) scan with a forced vital capacity (FVC) of less than 70% predicted. If an HRCT scan was not performed, which was the case for 88 (27%) patients at baseline, one of the following criteria was sufficient to diagnose pulmonary fibrosis: chest X-ray confirmed bibasal shadowing, FVC<55% predicted or DLCO (carbon monoxide diffusing capacity) <55% predicted.
Pulmonary hypertension	Raised mean pulmonary artery pressure at right heart catheterisation (greater than 25mmHg) or an estimated systolic pulmonary artery pressure (sPAP)/right ventricular systolic pressure (RVSP) of > 40mmg Hg on echocardiography (or > 45 mmHg including right atrial pressure [RAP] if the measure included RAP, but the value of this was not stated).
Cardiac involvement	Haemodynamically significant cardiac arrhythmia, pericardial effusion or congestive cardiac failure requiring hospitalisation or specific drug treatment, diastolic dysfunction (diagnosed usually on echocardiogram), ejection fraction less than 50%, or other cardiac manifestation felt to be clinically significant as judged by the investigators.
Renal crisis	Defined on the basis of clinician opinion and at least one of: decrease in estimated glomerular filtration rate (eGFR) by 30%, new onset blood pressure > 150/90 mmHg, microangiopathic haemolytic anaemia, retinopathy or renal biopsy findings.
Renal impairment	Defined as mild (eGFR 60-89 ml/min), moderate (30-59ml/min) and severe (< 29ml/min). Furthermore, a separate classification labelled "Renal involvement" was categorized as the presence of renal crisis and/or moderate-to-severe renal impairment.
Gastrointestinal involvement	Present if any of the following: weight loss more than 10% in the preceding 6 months, oesophageal dysmotility (on barium swallow or manometry), malabsorption, severe constipation, faecal incontinence, or rectal prolapse. If a patient had had more than 3 episodes of intestinal pseudo-obstruction, or more than 6 weeks' nutritional support, then a diagnosis of 'advanced gastrointestinal involvement' was made. A category labelled "Any gastrointestinal involvement" included patients with any kind of gastrointestinal involvement cited above.
Muscle involvement	One or more of the following: creatine kinase (CK) more than 4 times normal, abnormal muscle biopsy, abnormal electromyography, or proximal muscle weakness combined with investigator opinion.

For each patient, the presence of organ involvement of any type was carried forward from the time of diagnosis until the time of study exit. That is, organ involvement (such as pulmonary fibrosis) was not assumed to be reversed once it was detected using the criteria outlined above. Conversely, for each category above, if the outlined criteria ruled out organ involvement and previous investigations during past visits were inconclusive, it was assumed that the patient never had this type of manifestation (the absence of organ involvement was carried backwards).

Supplementary Table S2. Primary and secondary outcome measures.

Clinical variables	Frequency of recording	Outcome variable
Modified Rodnan skin score (mRSS)	3 monthly	mRSS (primary)
Haemoglobin Erythrocyte sedimentation rate (ESR) Plasma creatinine Estimated glomerular filtration rate (eGFR) C-Reactive protein (CRP)	3 monthly	Outcomes assessed in a preliminary analysis but not included as secondary outcomes.
High-resolution computed tomography (HRCT) findings Forced vital capacity (FVC - % predicted) Carbon monoxide diffusing capacity (DLCO - % predicted) Estimated systolic pulmonary arterial pressure (sPAP) / right ventricular systolic pressure (RVSP)	12 monthly (except HRCT)	FVC (secondary) DLCO (secondary)
Scleroderma Specific Health Assessment Questionnaire [sHAQ], including HAQ-DI disability index FACIT fatigue score Short Form 36 Health Survey (SF36) Cochin Hand Function Scale	12 monthly	HAQ-DI (secondary) Cochin Hand Function Scale (secondary)
Side effects from primary disease-modifying treatment	3 monthly	Side effects (secondary)
Survival	Date and cause of death recorded	Survival (secondary)

Supplementary Table S3. Doses by protocol.

		Baseline		12 months		24 months	
	Frequency	n	Median dose in mg (IQR)	n	Median dose in mg (IQR)	n	Median dose in mg (IQR)
Methotrexate							
Oral	Weekly	44	15 (10-20)	20	17 (15-20)	15	15 (13-20)
Subcutaneous	Weekly	13	15 (15-20)	7	15 (10-20)	6	15 (10-15)
Intramuscular	Weekly	8	10 (10-15)	7	10 (10-15)	7	10 (10-15)
Mycophenolate mofetil							
Oral	Daily	118	1000 (1000-2000)	92	2000 (1000-2000)	55	2000 (1000-2000)
Cyclophosphamide							
Oral	Daily	4	100 (100-1050)	2	100 (100-100)	2	100 (100-100)
Intravenous	Approx. monthly	82	1000 (750-1221)	23	1200 (1000-1353)	3	400 (267-1000)

At 12 and 24 months, doses are shown for patients who remained on the same drug and route combination as baseline

Supplementary Table S4. Use of concomitant medications, no. (% of drug family)

	At baseline	During study
Endothelin receptor antagonists	12 (3.7*)	35 (10.7*)
Bosentan	11 (91.7)	32 (91.4)
Other	1 (8.3)	5 (14.2)
Calcium channel blockers	128 (39.5*)	185 (56.8*)
Musculoskeletal	73 (22.5*)	130 (39.9*)
NSAIDs	42 (57.5)	69 (53.1)
Analgesics	4 (5.5)	7 (5.4)
Hydroxychloroquine[(a)]	25 (34.2)	49 (37.7)
Methotrexate (not as main treatment protocol)	0 (0)	2 (1.5)
Tocilizumab for inflammatory arthritis	0 (0)	1 (0.8)
Other	3 (4.1)	28 (21.5)
Renal	51 (15.9*)	88 (27.1*)
ACE inhibitors	46 (90.2)	79 (89.8)
Other	12 (23.5)	28 (31.8)
Gastrointestinal	224 (70*)	289 (88.7*)
Proton pump inhibitors	216 (96.4)	285 (98.6)
H2 blockers	10 (4.5)	40 (13.8)
Antacid	12 (5.4)	41 (14.2)
Broad spectrum antibiotics for bacterial overgrowth	4 (1.8)	14 (4.8)
Prokinetic drugs	21 (9.4)	69 (23.9)
Other	10 (4.5)	34 (11.8)
Anti-platelet agents	58 (18.2*)	98 (30.1*)
Aspirin	55 (94.8)	84 (85.7)
Other	5 (8.6)	18 (18.4)
Angiotensin II receptor antagonists	27 (8.3*)	52 (16*)
IV-prostanoids [(ab)]	53 (17.2*)	108 (33.1*)

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* As a % of entire cohort (326 patients)

(a) Out of the 25 patients receiving hydroxychloroquine at baseline, 12 received~~were assigned to~~ MMF, 9 ~~to~~ cyclophosphamide and 4 ~~to~~ 'no immunosuppressant'.

(ba) IV prostanoids prior to study entry

Supplementary Table S5. Confounders included in each analysis.

Outcome	Potential confounders (for treatment allocation and censoring)
mRSS	Age, Months since onset of skin thickening, cCurrent or previous steroid use, Anti-topoisomerase (anti-Scl70), Anti-RNA polymerase III, Pulmonary fibrosis, Pulmonary hypertension, Cardiac involvement, Renal involvement, Muscle involvement, HAQ-DI, FACIT fatigue score, Cochin Hand Function Scale
FVC	Age, Female, Previous immunosuppressant use, Current or previous steroid use, mRSS, Anti-topoisomerase (anti-Scl70), Anti-RNA polymerase III, Anticentromere, Pulmonary fibrosis, Pulmonary hypertension, Cardiac involvement, Renal involvement, Muscle involvement, HAQ-DI, FACIT fatigue score, Cochin Hand Function Scale
FVC (subset with pulmonary fibrosis on HRCT scan at baseline)	Age, Female, Current or previous steroid use, mRSS, Pulmonary fibrosis, Pulmonary hypertension, Renal involvement, HAQ-DI, FACIT fatigue score
DLCO	Age, Female, Current or previous steroid use, Anti-topoisomerase (anti-Scl70), Anti-RNA polymerase III, Anticentromere, Pulmonary fibrosis, Pulmonary hypertension, Cardiac involvement, Renal involvement, HAQ-DI, FACIT fatigue score, Cochin Hand Function Scale
DLCO (subset with pulmonary fibrosis on HRCT scan at baseline)	Current or previous steroid use, Pulmonary fibrosis, Pulmonary hypertension, Cardiac involvement, Renal involvement, HAQ-DI, FACIT fatigue score
HAQ-DI	Previous immunosuppressant use, Current or previous steroid use, mRSS, Anticentromere, Pulmonary fibrosis, Pulmonary hypertension, Cardiac involvement, Muscle involvement, FACIT fatigue score, Cochin Hand Function Scale
Cochin Hand Function Scale	Current or previous steroid use, mRSS, Pulmonary fibrosis, Muscle involvement, HAQ-DI, FACIT fatigue score
Survival	Age, mRSS, Pulmonary fibrosis, Pulmonary hypertension, Cardiac involvement, Renal involvement, HAQ-DI, FACIT fatigue score, Cochin Hand Function Scale
Event-free survival (protocol change due to adverse effects)	None

The criterion for inclusion as a potential confounder was association with the outcome variable, as detailed in Supplementary Tables 6 to 13 for the different models.

DLCO: Carbon monoxide diffusing capacity
FVC: Forced vital capacity
HAQ-DI: Health Assessment Questionnaire - Disability Index
HRCT: High resolution computed tomography
mRSS: modified Rodnan skin score (17 sites)
RVSP: Right ventricular systolic pressure
sPAP: Systolic pulmonary artery pressure

Supplementary Table S6. Confounder selection for skin score (mRSS).

mRSS	(A) Association with outcome at baseline		(B) Effect on outcome through time					
	Baseline predictor, coefficient (95% CI)	p[(1)]	Time slope (12 months)	Time-predictor interaction, coefficient (95% CI)	p[(2)]	Between group difference, p[(3)]	Potential confounder	Retained
Age, years	0.1 (0 to 0.2)	0.004	-1.8	0 (-0.1 to 0)	0.007	0.324	Y	Y
Female, no.	-1.8 (-3.7 to 0.2)	0.072	-3.5	0.1 (-0.5 to 0.8)	0.680	0.003		
Months since onset of skin thickening	-0.1 (-0.2 to 0)	0.156	-4.3	0.1 (0 to 0.1)	0.002	0.001	Y	Y
Previous immunosuppressant use	-2.1 (-5.3 to 1.2)	0.205	-3.5	0.1 (-1 to 1.3)	0.808	0.007		
Current or previous steroid use	1.2 (-0.6 to 3)	0.191	-2.9	-1.2 (-1.8 to -0.6)	<0.0005	0.001	Y	Y
mRSS			0.9	-0.2 (-0.2 to -0.2)	<0.0001	0.306		
Haemoglobin g/l *	-0.1 (-0.1 to 0)	0.003	-5.8	0 (0 to 0)	0.074	0.721	Y	
White blood count (WBC) x10^9/l *	0.5 (0.2 to 0.8)	0.002	-2.2	-0.1 (-0.3 to 0)	0.014	0.029	Y	
Platelets x10^9/l *	0 (0 to 0)	0.001	-3.1	0 (0 to 0)	0.546	0.459	Y	
ESR mm/hr *	0.1 (0 to 0.1)	0.003	-4	0 (0 to 0)	0.079	0.341	Y	
CRP mg/l *	0.1 (0 to 0.2)	0.003	-4.4	0.1 (0 to 0.1)	0.001	0.026	Y	
Anti-topoisomerase (anti-Scl70)	-2.6 (-4.4 to -0.8)	0.005	-4.3	2.2 (1.6 to 2.8)	<0.0001	0.228	Y	Y
Anti-RNA polymerase III	4.5 (2.1 to 6.9)	<0.0005	-3	-2.1 (-2.9 to -1.2)	<0.0001	0.433	Y	Y
Anticentromere	-0.4 (-3.9 to 3.1)	0.816	-3.4	0.5 (-0.8 to 1.9)	0.456	0.147		
Pulmonary fibrosis	2.9 (0.4 to 5.4)	0.021	-3.5	0.3 (-0.6 to 1.2)	0.534	0.036	Y	Y
FVC (% predicted) **	-0.1 (-0.1 to 0)	0.013	-5.5	0 (0 to 0)	0.005	0.026	Y	
DLCO (% predicted) **	0 (-0.1 to 0)	0.105	-3.2	0 (0 to 0)	0.689	<0.0005		
Pulmonary hypertension	2.5 (-0.7 to 5.8)	0.128	-3.3	-2.1 (-3.3 to -0.8)	0.001	0.488	Y	Y
sPAP or RVSP mmHg **	0.1 (0 to 0.2)	0.151	-2.2	0 (-0.1 to 0)	0.018	0.472	Y	
Cardiac involvement	2.5 (-0.2 to 5.2)	0.075	-3.5	0 (-1 to 0.9)	0.929	0.009		Y
Renal involvement	2.2 (-0.7 to 5.2)	0.140	-3.3	-1.6 (-2.6 to -0.5)	0.004	0.039	Y	Y
eGFR ml/min **	0 (-0.1 to 0)	0.383	-5.4	0 (0 to 0)	0.007	0.339	Y	
Renal crisis **	0.5 (-3.6 to 4.6)	0.799	-3.4	-1.5 (-3.1 to 0.1)	0.062	0.110		
Plasma creatinine in µmol/l *	0 (0 to 0)	0.882	-3.5	0 (0 to 0)	0.687	0.422		
Any GI involvement *	2.2 (0.3 to 4)	0.021	-3.4	-0.1 (-0.8 to 0.5)	0.664	0.078	Y	
Muscle involvement	1.2 (-1.8 to 4.2)	0.425	-3.2	-2 (-2.9 to -1)	<0.0005	0.002	Y	Y
Current digital ulcers *	2.5 (0.1 to 4.8)	0.038	-3.3	-0.9 (-1.8 to 0)	0.047	0.705	Y	
HAQ-DI Disability index (0-3)	3.5 (2.5 to 4.6)	<0.0001	-3	-0.4 (-0.8 to 0)	0.039	0.400	Y	Y
FACIT fatigue score (0-52)	-0.1 (-0.2 to -0.1)	<0.0005	-3.1	0 (0 to 0)	0.484	0.165	Y	Y
Cochin Hand Function Scale (0-90)	0.1 (0.1 to 0.2)	<0.0001	-3.7	0 (0 to 0)	0.979	0.025	Y	Y

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.
** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal
HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)

$p^{(1)}$: significance p-value for characteristic coefficient in linear regression of baseline outcome on baseline predictor
$p^{(2)}$: significance p-value for interaction coefficient between time and baseline characteristic in a longitudinal regression model
$p^{(3)}$: p-value from Fisher's or Kruskal-Wallis test

Supplementary Table S7. Confounder selection for FVC.

FVC	**(A) Association with outcome at baseline**		**(B) Effect on outcome through time**					
	Baseline predictor, coefficient (95% CI)	$p^{(1)}$	Time slope (12 months)	Time-predictor interaction, coefficient (95% CI)	$p^{(2)}$	Between group difference, $p^{(3)}$	Potential confounder	Retained
Age, years	0.1 (-0.1 to 0.2)	0.509	-4.8	0.1 (0.1 to 0.2)	<0.0001	0.324	Y	Y
Female, no.	6.0 (1.1 to 10.9)	0.017	1.9	-1.5 (-3.2 to 0.2)	0.077	0.003	Y	Y
Months since onset of skin thickening	-0.2 (-0.5 to 0)	0.067	0.8	0 (-0.1 to 0.1)	0.824	0.001		
Previous immunosuppressant use	-3 (-11.2 to 5.1)	0.462	1	-3.1 (-5.8 to -0.4)	0.024	0.007	Y	Y
Current or previous steroid use	-6.1 (-10.7 to -1.5)	0.009	0.5	0.8 (-0.7 to 2.4)	0.299	0.001	Y	Y
mRSS	-0.4 (-0.6 to -0.1)	0.013	0.4	0 (-0.1 to 0.1)	0.712	0.306	Y	Y
Haemoglobin g/l *	0.1 (-0.1 to 0.2)	0.231	8.1	-0.1 (-0.1 to 0)	0.025	0.721	Y	
White blood count (WBC) $x10^9$/l *	-1.1 (-1.9 to -0.3)	0.009	-2.2	0.4 (0.1 to 0.6)	0.008	0.029	Y	
Platelets $x10^9$/l *	0 (0 to 0)	0.593	-0.7	0 (0 to 0)	0.239	0.459		
ESR mm/hr *	-0.2 (-0.3 to -0.1)	0.005	-0.1	0 (0 to 0.1)	0.051	0.341	Y	
CRP mg/l *	-0.1 (-0.2 to 0.1)	0.352	2	-0.1 (-0.1 to 0)	0.160	0.026		
Anti-topoisomerase (anti-Scl70)	-4.8 (-9.5 to -0.2)	0.043	1.6	-1.6 (-3.1 to -0.1)	0.042	0.228	Y	Y
Anti-RNA polymerase III	9.4 (3.2 to 15.7)	0.003	0.6	-0.5 (-2.5 to 1.5)	0.615	0.433	Y	Y
Anticentromere	12.9 (3.8 to 22.1)	0.006	1	-2.5 (-6.0 to 0.9)	0.152	0.147	Y	Y
Pulmonary fibrosis	-31.2 (-36.4 to -26.0)	<0.0001	0.2	4.6 (2.4 to 6.8)	<0.0001	0.036	Y	Y
FVC (% predicted) **				-0.1 (-0.2 to -0.1)	<0.0001	0.026		
DLCO (% predicted) **	0.6 (0.5 to 0.7)	<0.0001	6.4	-0.1 (-0.1 to 0)	<0.0001	<0.0005	Y	
Pulmonary hypertension	-16.8 (-24.8 to -8.7)	<0.0001	0.5	3.8 (0.8 to 6.8)	0.014	0.488	Y	Y
sPAP or RVSP mmHg **	-0.4 (-0.6 to -0.2)	0.001	-2.1	0.1 (0 to 0.2)	0.005	0.472	Y	
Cardiac involvement	-11.7 (-18.5 to -4.8)	0.001	0.5	2.2 (-0.1 to 4.6)	0.059	0.009	Y	Y

Renal involvement	-2.2 (-10.0 to 5.5)	0.572	0.3	5.4 (2.8 to 8.1)	<0.0001	0.039	Y	Y
eGFR ml/min **	0 (-0.1 to 0.1)	0.609	7.3	-0.1 (-0.1 to 0)	<0.0001	0.339	Y	
Renal crisis **	0.4 (-10.8 to 11.7)	0.940	0.6	6.6 (2.2 to 11.0)	0.003	0.11	Y	
Plasma creatinine in µmol/l *	0 (-0.1 to 0)	0.300	0.1	0 (0 to 0)	0.010	0.422	Y	
Any GI involvement *	-4.1 (-8.8 to 0.7)	0.094	0.2	1.6 (0 to 3.1)	0.051	0.078	Y	
Muscle involvement	-8.2 (-15.8 to -0.6)	0.034	0.6	1.5 (-0.8 to 3.9)	0.204	0.002	Y	Y
Current digital ulcers *	-3.6 (-9.8 to 2.6)	0.255	1.1	-2.2 (-4.4 to -0.1)	0.041	0.705	Y	
HAQ-DI Disability index (0-3)	-6 (-8.7 to -3.2)	<0.0001	0.8	-0.1 (-1.0 to 0.9)	0.897	0.4	Y	Y
FACIT fatigue score (0-52)	0.4 (0.2 to 0.5)	<0.0001	0.2	0 (0 to 0.1)	0.638	0.165	Y	Y
Cochin Hand Function Scale (0-90)	-0.2 (-0.3 to 0)	0.009	1.2	0 (-0.1 to 0)	0.724	0.025	Y	Y

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.
** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal
HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)

$p^{(1)}$: significance p-value for characteristic coefficient in linear regression of baseline outcome on baseline predictor
$p^{(2)}$: significance p-value for interaction coefficient between time and baseline characteristic in a longitudinal regression model
$p^{(3)}$: p-value from Fisher's or Kruskal-Wallis test

Supplementary Table S8. Confounder selection for FVC, subset.

FVC, subset with pulmonary fibrosis on HRCT scan	**(A) Association with outcome at baseline**		**(B) Effect on outcome through time**					
	Baseline predictor, coefficient (95% CI)	$p^{(1)}$	Time slope (12 months)	Time-predictor interaction, coefficient (95% CI)	$p^{(2)}$	Between group difference, $p^{(3)}$	Potential confounder	Retained
Age, years	0.1 (-0.2 to 0.3)	0.587	-5.3	0.1 (0 to 0.2)	0.013	0.324	Y	Y
Female, no.	3.8 (-3.3 to 11.0)	0.287	3.8	-3.6 (-6.1 to -1)	0.006	0.003	Y	Y
Months since onset of skin thickening	0 (-0.3 to 0.4)	0.839	2.4	-0.1 (-0.2 to 0.1)	0.444	0.001		
Previous immunosuppressant use	-2.7 (-14.0 to 8.5)	0.633	1.6	-2.6 (-6.7 to 1.4)	0.198	0.007		
Current or previous steroid use	-6.8 (-13.5 to 0)	0.048	0.7	1.2 (-1.2 to 3.6)	0.331	0.001	Y	Y
mRSS	-0.5 (-0.9 to -0.2)	0.006	0.2	0.1 (-0.1 to 0.2)	0.513	0.306	Y	Y
Haemoglobin g/l *	0.2 (0 to 0.4)	0.104	4.5	0 (-0.1 to 0.1)	0.529	0.721		
White blood count (WBC) x10^9/l *	-1.3 (-2.3 to -0.2)	0.021	-6.2	0.9 (0.5 to 1.2)	<0.0001	0.029	Y	
Platelets x10^9/l *	0 (-0.1 to 0)	0.094	-5	0 (0 to 0)	0.001	0.459	Y	
ESR mm/hr *	-0.3 (-0.4 to -0.1)	0.005	-1.3	0.1 (0 to 0.2)	0.017	0.341	Y	

CRP mg/l *	-0.1 (-0.3 to 0.1)	0.250	2.4	0 (-0.2 to 0.1)	0.602	0.026		
Anti-topoisomerase (anti-Scl70)	-0.9 (-7.9 to 6)	0.792	2.3	-1.5 (-3.9 to 0.9)	0.224	0.228		
Anti-RNA polymerase III	11.3 (-2.6 to 25.1)	0.109	1.1	-0.9 (-5 to 3.1)	0.651	0.433		
Anticentromere	4.5 (-13.3 to 22.4)	0.616	1.6	-3.1 (-9.3 to 3.2)	0.334	0.147		
Pulmonary fibrosis	-27.8 (-32.8 to -22.7)	<0.0001	-0.3	5.2 (2.6 to 7.7)	<0.0001	0.036	Y	Y
FVC (% predicted) **			12.9	-0.1 (-0.2 to -0.1)	<0.0001	0.026		
DLCO (% predicted) **	0.5 (0.4 to 0.7)	<0.0001	5.2	-0.1 (-0.1 to 0)	0.070	<0.0005	Y	
Pulmonary hypertension	-13.0 (-22.1 to -4.0)	0.005	1.1	1.9 (-1.6 to 5.4)	0.297	0.488	Y	Y
sPAP or RVSP mmHg **	-0.2 (-0.5 to 0)	0.097	-1	0.1 (0 to 0.2)	0.089	0.472		
Cardiac involvement	-6.8 (-15.1 to 1.4)	0.103	0.9	2.0 (-0.9 to 5)	0.176	0.009		
Renal involvement	-0.4 (-11.3 to 10.5)	0.944	0.6	6.8 (3 to 10.7)	<0.0005	0.039	Y	Y
eGFR ml/min **	0 (-0.2 to 0.1)	0.650	8.4	-0.1 (-0.1 to 0)	0.007	0.339	Y	
Renal crisis **	-2.6 (-20.1 to 15)	0.771	1	12.3 (5.2 to 19.5)	0.001	0.110	Y	
Plasma creatinine in µmol/l *	0 (-0.1 to 0)	0.271	-0.1	0 (0 to 0)	0.009	0.422	Y	
Any GI involvement *	-2.5 (-9.3 to 4.3)	0.462	0.6	1.6 (-0.8 to 4)	0.188	0.078		
Muscle involvement	-3.4 (-13.7 to 6.9)	0.514	0.9	2.9 (-0.6 to 6.3)	0.102	0.002		
Current digital ulcers *	-6.9 (-16.1 to 2.4)	0.146	1.5	-1.9 (-5.8 to 2.1)	0.357	0.705		
HAQ-DI Disability index (0-3)	-6.9 (-10.7 to -3.1)	0.001	1.6	-0.5 (-2 to 1)	0.521	0.400	Y	Y
FACIT fatigue score (0-52)	0.5 (0.2 to 0.7)	<0.0005	0.6	0 (-0.1 to 0.1)	0.740	0.165	Y	Y
Cochin Hand Function Scale (0-90)	-0.2 (-0.4 to 0)	0.106	2	0 (-0.1 to 0.1)	0.623	0.025		

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.
** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal
HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)

$p^{(1)}$: significance p-value for characteristic coefficient in linear regression of baseline outcome on baseline predictor
$p^{(2)}$: significance p-value for interaction coefficient between time and baseline characteristic in a longitudinal regression model
$p^{(3)}$: p-value from Fisher's or Kruskal-Wallis test

Supplementary Table S9. Confounder selection for DLCO.

DLCO	**(A) Association with outcome at baseline**	**(B) Effect on outcome through time**

	Baseline predictor, coefficient (95% CI)	p(1)	Time slope (12 months)	Time-predictor interaction, coefficient (95% CI)	p(2)	Between group difference, p(3)	Potential confounder	Retained
Age, years	-0.2 (-0.3 to 0)	0.034	-3.3	0.1 (0 to 0.1)	0.068	0.324	Y	Y
Female, no.	6.4 (1.7 to 11.1)	0.008	0	-0.5 (-2.3 to 1.4)	0.619	0.003	Y	Y
Months since onset of skin thickening	-0.2 (-0.5 to 0)	0.068	-0.7	0 (-0.1 to 0.1)	0.389	0.001		
Previous immunosuppressant use	-5.9 (-13.5 to 1.8)	0.133	-0.3	-0.5 (-3.4 to 2.4)	0.748	0.007		
Current or previous steroid use	-6 (-10.4 to -1.6)	0.008	-1.2	1.8 (0.1 to 3.5)	0.033	0.001	Y	Y
mRSS	-0.2 (-0.5 to 0)	0.105	-0.5	0 (-0.1 to 0.1)	0.863	0.306		
Haemoglobin g/l *	0.2 (0 to 0.3)	0.027	7	-0.1 (-0.1 to 0)	0.040	0.721	Y	
White blood count (WBC) x10^9/l *	-1.4 (-2.2 to -0.6)	0.001	-1.4	0.1 (-0.2 to 0.4)	0.418	0.029	Y	
Platelets x10^9/l *	0 (0 to 0)	0.035	-0.1	0 (0 to 0)	0.887	0.459	Y	
ESR mm/hr *	-0.2 (-0.3 to -0.1)	0.002	-0.5	0 (-0.1 to 0.1)	0.941	0.341	Y	
CRP mg/l *	-0.3 (-0.4 to -0.1)	0.003	0	0 (-0.2 to 0.1)	0.348	0.026	Y	
Anti-topoisomerase (anti-Scl70)	-5.9 (-10.4 to -1.5)	0.009	0.2	-1.4 (-3.1 to 0.3)	0.106	0.228	Y	Y
Anti-RNA polymerase III	6.5 (0.6 to 12.4)	0.031	-0.6	0.7 (-1.5 to 2.9)	0.520	0.433	Y	Y
Anticentromere	8.6 (-0.2 to 17.3)	0.054	-0.4	-1.1 (-5 to 2.8)	0.582	0.147		Y
Pulmonary fibrosis	-21 (-27.2 to -14.8)	<0.0001	-0.6	2.1 (-0.5 to 4.8)	0.116	0.036	Y	Y
FVC (% predicted) **	0.6 (0.5 to 0.7)	<0.0001	5.4	-0.1 (-0.1 to 0)	0.007	0.026	Y	
DLCO (% predicted) **			9.6	-0.2 (-0.2 to -0.1)	<0.0001	<0.0005		
Pulmonary hypertension	-16 (-24.9 to -7.1)	<0.0005	-0.5	3.2 (-0.6 to 6.9)	0.097	0.488	Y	Y
sPAP or RVSP mmHg **	-0.5 (-0.7 to -0.3)	<0.0001	-2.9	0.1 (0 to 0.1)	0.039	0.472	Y	
Cardiac involvement	-8.2 (-15.1 to -1.2)	0.021	-0.6	2.6 (-0.1 to 5.2)	0.058	0.009	Y	Y
Renal involvement	-7.4 (-14.8 to 0)	0.049	-0.6	3.4 (0.5 to 6.4)	0.021	0.039	Y	Y
eGFR ml/min **	0 (-0.1 to 0.1)	0.337	2.8	0 (-0.1 to 0)	0.044	0.339	Y	
Renal crisis **	-11.6 (-22.1 to -1.1)	0.031	-0.6	8.2 (3.7 to 12.7)	<0.0005	0.110	Y	
Plasma creatinine in µmol/l *	0 (-0.1 to 0)	0.008	-1.2	0 (0 to 0)	0.013	0.422	Y	
Any GI involvement *	-1.6 (-6.3 to 3.1)	0.498	-0.7	1.1 (-0.6 to 2.9)	0.195	0.078		
Muscle involvement	-3.8 (-11.7 to 4.2)	0.351	-0.5	1.3 (-1.4 to 4)	0.358	0.002		
Current digital ulcers *	-3.8 (-9.9 to 2.3)	0.218	-0.3	-0.4 (-2.8 to 2)	0.759	0.705		
HAQ-DI Disability index (0-3)	-5.4 (-8.1 to -2.7)	<0.0005	0	-0.4 (-1.5 to 0.6)	0.410	0.400	Y	Y
FACIT fatigue score (0-52)	0.3 (0.2 to 0.5)	<0.0005	-2.1	0.1 (0 to 0.1)	0.130	0.165	Y	Y
Cochin Hand Function Scale (0-90)	-0.2 (-0.3 to -0.1)	0.006	0.2	0 (-0.1 to 0)	0.617	0.025	Y	Y

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.

** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal
HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)

$p^{(1)}$: significance p-value for characteristic coefficient in linear regression of baseline outcome on baseline predictor
$p^{(2)}$: significance p-value for interaction coefficient between time and baseline characteristic in a longitudinal regression model
$p^{(3)}$: p-value from Fisher's or Kruskal-Wallis test

Supplementary Table S10. Confounder selection for DLCO, subset.

DLCO, subset with pulmonary fibrosis on HRCT scan	**(A) Association with outcome at baseline**		**(B) Effect on outcome through time**					
	Baseline predictor, coefficient (95% CI)	$p^{(1)}$	Time slope (12 months)	Time-predictor interaction, coefficient (95% CI)	$p^{(2)}$	Between group difference, $p^{(3)}$	Potential confounder	Retained
Age, years	-0.1 (-0.3 to 0.2)	0.542	-0.9	0 (-0.1 to 0.1)	0.496	0.324		
Female, no.	4.3 (-2.6 to 11.3)	0.221	0.6	0.5 (-2.1 to 3)	0.712	0.003		
Months since onset of skin thickening	-0.3 (-0.6 to 0.1)	0.132	1.8	0 (-0.2 to 0.1)	0.644	0.001		
Previous immunosuppressant use	-1.1 (-11.7 to 9.4)	0.832	0.8	1.2 (-2.5 to 5.0)	0.520	0.007		
Current or previous steroid use	-5.2 (-11.9 to 1.4)	0.123	-0.3	2.3 (0 to 4.7)	0.050	0.001	Y	Y
mRSS	-0.3 (-0.7 to 0.1)	0.118	1.3	0 (-0.2 to 0.1)	0.815	0.306		
Haemoglobin g/l *	0.1 (-0.1 to 0.3)	0.147	7.2	0 (-0.1 to 0)	0.188	0.721		
White blood count (WBC) $x10^9$/l *	-0.9 (-2 to 0.2)	0.108	1.7	-0.1 (-0.4 to 0.3)	0.686	0.029		
Platelets $x10^9$/l *	0 (-0.1 to 0)	0.018	-0.2	0 (0 to 0)	0.509	0.459	Y	
ESR mm/hr *	-0.1 (-0.3 to 0)	0.128	-1.1	0 (0 to 0.1)	0.335	0.341		
CRP mg/l *	-0.2 (-0.4 to 0)	0.077	0.5	0 (-0.1 to 0.1)	0.901	0.026		
Anti-topoisomerase (anti-Scl70)	-3.0 (-9.8 to 3.7)	0.376	1.4	-1.0 (-3.4 to 1.4)	0.403	0.228		
Anti-RNA polymerase III	9.3 (-2.7 to 21.3)	0.126	0.5	3.3 (-0.7 to 7.4)	0.104	0.433		
Anticentromere	2.9 (-15.4 to 21.2)	0.751	0.8	0.6 (-5.9 to 7.2)	0.851	0.147		
Pulmonary fibrosis	-12.6 (-19.4 to -5.8)	<0.0005	0.7	0.7 (-2 to 3.3)	0.610	0.036	Y	Y
FVC (% predicted) **	0.5 (0.4 to 0.7)	<0.0001	1.3	0 (-0.1 to 0.1)	0.934	0.026	Y	
DLCO (% predicted) **			7.2	-0.1 (-0.2 to 0)	0.001	0.000		
Pulmonary hypertension	-15.4 (-25.2 to -5.6)	0.002	0.6	2.9 (-0.7 to 6.6)	0.117	0.488	Y	Y
sPAP or RVSP mmHg **	-0.4 (-0.7 to -0.2)	0.002	-1.5	0.1 (0 to 0.1)	0.144	0.472	Y	
Cardiac involvement	-1.5 (-10 to 6.9)	0.721	0.3	3.5 (0.5 to 6.4)	0.023	<0.0005	Y	Y
Renal involvement	2.0 (-9 to 12.9)	0.723	0.5	4.0 (0.1 to 8.0)	0.045	0.039	Y	Y
eGFR ml/min **	0 (-0.2 to 0.1)	0.680	6.1	-0.1 (-0.1 to 0)	0.023	0.339	Y	

Renal crisis **	-3.2 (-21.4 to 15.0)	0.730	0.6	9.1 (2.5 to 15.7)	0.007	0.110	Y	
Plasma creatinine in µmol/l *	0 (-0.1 to 0)	0.197	0.6	0 (0 to 0)	0.057	0.422		
Any GI involvement *	1.5 (-5.3 to 8.2)	0.667	0.5	1.1 (-1.3 to 3.4)	0.377	0.078		
Muscle involvement	7.2 (-3.3 to 17.6)	0.176	1.2	-2.3 (-5.8 to 1.2)	0.198	0.002		
Current digital ulcers *	-4.1 (-13.7 to 5.6)	0.405	0.9	0.4 (-3.7 to 4.5)	0.852	0.705		
HAQ-DI Disability index (0-3)	-4.6 (-8.5 to -0.7)	0.020	1.2	-0.6 (-2.2 to 0.9)	0.422	0.400	Y	Y
FACIT fatigue score (0-52)	0.3 (0.1 to 0.6)	0.009	-0.1	0 (-0.1 to 0.1)	0.555	0.165	Y	Y
Cochin Hand Function Scale (0-90)	-0.1 (-0.3 to 0.1)	0.232	1.3	0 (-0.1 to 0.1)	0.972	0.025		

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.
** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal
HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)

$p^{(1)}$: significance p-value for characteristic coefficient in linear regression of baseline outcome on baseline predictor
$p^{(2)}$: significance p-value for interaction coefficient between time and baseline characteristic in a longitudinal regression model
$p^{(3)}$: p-value from Fisher's or Kruskal-Wallis test

Supplementary Table S11. Confounder selection for HAQ-DI.

HAQ-DI	**(A) Association with outcome at baseline**		**(B) Effect on outcome through time**					
	Baseline predictor, coefficient (95% CI)	$p^{(1)}$	Time slope (12 months)	Time-predictor interaction, coefficient (95% CI)	$p^{(2)}$	Between group difference, $p^{(3)}$	Potential confounder	Retained
Age, years	0 (-0.01 to 0)	0.568	-0.12	0 (0 to 0)	0.182	0.324		
Female, no.	0.18 (-0.03 to 0.38)	0.090	-0.02	0 (-0.09 to 0.09)	0.963	0.003		
Months since onset of skin thickening	0 (-0.01 to 0.01)	0.874	-0.04	0 (0 to 0.01)	0.561	0.001		
Previous immunosuppressant use	0.09 (-0.26 to 0.44)	0.619	-0.01	-0.19 (-0.34 to -0.03)	0.016	0.007	Y	Y
Current or previous steroid use	0.31 (0.13 to 0.5)	0.001	0.02	-0.09 (-0.17 to -0.02)	0.020	0.001	Y	Y
mRSS	0.04 (0.03 to 0.05)	<0.0001	0.03	0 (-0.01 to 0)	0.427	0.306	Y	Y
Haemoglobin g/l *	-0.02 (-0.02 to -0.01)	<0.0005	-0.25	0 (0 to 0)	0.179	0.721	Y	
White blood count (WBC) x10^9/l *	0.03 (-0.01 to 0.06)	0.098	-0.02	0 (-0.01 to 0.01)	0.947	0.029		
Platelets x10^9/l *	0 (0 to 0)	<0.0005	-0.03	0 (0 to 0)	0.887	0.459	Y	
ESR mm/hr *	0.01 (0.01 to 0.02)	<0.0001	0	0 (0 to 0)	0.949	0.341	Y	
CRP mg/l *	0.02 (0.01 to 0.02)	<0.0001	-0.03	0 (0 to 0)	0.731	0.026	Y	

Anti-topoisomerase (anti-Scl70)	-0.08 (-0.28 to 0.11)	0.400	-0.03	0.03 (-0.05 to 0.11)	0.475	0.228		
Anti-RNA polymerase III	0.18 (-0.08 to 0.44)	0.183	-0.03	0.02 (-0.09 to 0.12)	0.747	0.433		
Anticentromere	-0.27 (-0.63 to 0.09)	0.137	-0.03	0.19 (0.02 to 0.35)	0.025	0.147	Y	Y
Pulmonary fibrosis	0.42 (0.14 to 0.7)	0.004	-0.03	0.09 (-0.03 to 0.21)	0.133	0.036	Y	Y
FVC (% predicted) **	-0.01 (-0.01 to -0.01)	<0.0001	-0.03	0 (0 to 0)	0.799	0.026	Y	
DLCO (% predicted) **	-0.01 (-0.01 to 0)	<0.0005	-0.04	0 (0 to 0)	0.625	<0.0005	Y	
Pulmonary hypertension	0.33 (-0.02 to 0.67)	0.063	-0.01	-0.15 (-0.32 to 0.02)	0.076	0.488		Y
sPAP or RVSP mmHg **	0.01 (0 to 0.01)	0.302	-0.01	0 (-0.01 to 0)	0.570	0.472		
Cardiac involvement	0.41 (0.13 to 0.69)	0.004	-0.01	-0.07 (-0.19 to 0.06)	0.321	0.009	Y	Y
Renal involvement	0.27 (-0.04 to 0.59)	0.087	-0.01	-0.11 (-0.25 to 0.03)	0.111	0.039		
eGFR ml/min **	0 (0 to 0)	0.891	-0.04	0 (0 to 0)	0.787	0.339		
Renal crisis **	-0.04 (-0.49 to 0.4)	0.849	-0.01	-0.15 (-0.38 to 0.08)	0.192	0.110		
Plasma creatinine in µmol/l *	0 (0 to 0)	0.477	-0.05	0 (0 to 0)	0.749	0.422		
Any GI involvement *	0.28 (0.09 to 0.48)	0.004	-0.01	-0.02 (-0.1 to 0.07)	0.677	0.078	Y	
Muscle involvement	0.54 (0.22 to 0.85)	0.001	0.01	-0.27 (-0.39 to -0.14)	<0.0001	0.002	Y	Y
Current digital ulcers *	0.39 (0.15 to 0.64)	0.002	0	-0.1 (-0.21 to 0.01)	0.078	0.705	Y	
HAQ-DI Disability index (0-3)			0.18	-0.19 (-0.23 to -0.14)	<0.0001	0.400		
FACIT fatigue score (0-52)	-0.04 (-0.05 to -0.04)	<0.0001	-0.15	0 (0 to 0.01)	0.011	0.165	Y	Y
Cochin Hand Function Scale (0-90)	0.03 (0.03 to 0.04)	<0.0001	0.02	0 (-0.01 to 0)	0.002	0.025	Y	Y

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.
** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal
HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)

$p^{(1)}$: significance p-value for characteristic coefficient in linear regression of baseline outcome on baseline predictor
$p^{(2)}$: significance p-value for interaction coefficient between time and baseline characteristic in a longitudinal regression model
$p^{(3)}$: p-value from Fisher's or Kruskal-Wallis test

Supplementary Table S12. Confounder selection for Cochin Hand Function Scale.

Log(Cochin score+1)	**(A) Association with outcome at baseline**		**(B) Effect on outcome through time**					
	Baseline predictor, coefficient (95% CI)	$p^{(1)}$	Time slope (12 months)	Time-predictor interaction, coefficient (95% CI)	$p^{(2)}$	Between group difference, $p^{(3)}$	Potential confounder	Retained

Age, years	0 (-0.02 to 0.01)	0.627	0.1	0 (-0.01 to 0)	0.187	0.324		
Female, no.	0.06 (-0.33 to 0.46)	0.755	0	0.03 (-0.13 to 0.18)	0.753	0.003		
Months since onset of skin thickening	0 (-0.02 to 0.02)	0.889	-0.1	0 (-0.01 to 0.01)	0.502	0.001		
Previous immunosuppressant use	0.13 (-0.56 to 0.81)	0.719	0	-0.11 (-0.4 to 0.17)	0.426	0.007		
Current or previous steroid use	0.43 (0.09 to 0.76)	0.014	0	-0.07 (-0.2 to 0.07)	0.337	0.001	Y	Y
mRSS	0.05 (0.04 to 0.07)	<0.0001	0	0 (-0.01 to 0.01)	0.879	0.306	Y	Y
Haemoglobin g/l *	-0.01 (-0.02 to 0)	0.019	-0.5	0 (0 to 0.01)	0.097	0.721	Y	
White blood count (WBC) x10^9/l *	0.03 (-0.03 to 0.09)	0.308	0	0 (-0.02 to 0.02)	0.982	0.029		
Platelets x10^9/l *	0 (0 to 0)	0.001	-0.1	0 (0 to 0)	0.590	0.459	Y	
ESR mm/hr *	0.01 (0 to 0.02)	0.003	0	0 (0 to 0)	0.456	0.341	Y	
CRP mg/l *	0.02 (0.01 to 0.04)	<0.0001	-0.1	0 (-0.01 to 0.01)	0.943	0.026	Y	
Anti-topoisomerase (anti-Scl70)	0.09 (-0.27 to 0.45)	0.608	0	0.09 (-0.05 to 0.23)	0.209	0.228		
Anti-RNA polymerase III	0.32 (-0.13 to 0.77)	0.160	0	0.02 (-0.16 to 0.19)	0.856	0.433		
Anticentromere	-0.41 (-1.04 to 0.21)	0.196	0	0.24 (-0.02 to 0.51)	0.073	0.147		
Pulmonary fibrosis	0.58 (0.05 to 1.12)	0.031	0	-0.01 (-0.24 to 0.22)	0.945	0.036	Y	Y
FVC (% predicted) **	-0.01 (-0.02 to 0)	0.004	0	0 (0 to 0)	0.725	0.026	Y	
DLCO (% predicted) **	-0.01 (-0.02 to 0)	0.014	-0.1	0 (0 to 0)	0.686	<0.0005	Y	
Pulmonary hypertension	-0.19 (-0.88 to 0.5)	0.585	0	-0.32 (-0.66 to 0.03)	0.070	0.488		
sPAP or RVSP mmHg **	0 (-0.02 to 0.01)	0.674	0.2	-0.01 (-0.02 to 0)	0.017	0.472	Y	
Cardiac involvement	0.32 (-0.27 to 0.91)	0.286	0	0.11 (-0.15 to 0.36)	0.409	0.009		
Renal involvement	0.33 (-0.25 to 0.9)	0.268	0	0.04 (-0.21 to 0.29)	0.739	0.039		
eGFR ml/min **	0 (-0.01 to 0.01)	0.683	0.1	0 (0 to 0)	0.540	0.339		
Renal crisis **	-0.15 (-0.91 to 0.62)	0.702	0	0.09 (-0.33 to 0.51)	0.681	0.110		
Plasma creatinine in µmol/l *	0 (0 to 0)	0.198	-0.1	0 (0 to 0)	0.088	0.422		
Any GI involvement *	0.18 (-0.2 to 0.56)	0.347	0	-0.04 (-0.2 to 0.11)	0.572	0.078		
Muscle involvement	0.52 (-0.1 to 1.13)	0.097	0	-0.36 (-0.59 to -0.13)	0.002	0.002	Y	Y
Current digital ulcers *	0.52 (0.06 to 0.99)	0.027	0	-0.01 (-0.2 to 0.19)	0.946	0.705	Y	
HAQ-DI Disability index (0-3)	1.24 (1.13 to 1.36)	<0.0001	0.1	-0.15 (-0.23 to -0.07)	<0.0005	0.400	Y	Y
FACIT fatigue score (0-52)	-0.06 (-0.07 to -0.05)	<0.0001	-0.1	0 (0 to 0.01)	0.168	0.165	Y	Y
Cochin Hand Function Scale (0-90)			0.1	-0.01 (-0.01 to 0)	<0.0001	0.025		

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.
** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal

HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)

$p^{(1)}$: significance p-value for characteristic coefficient in linear regression of baseline outcome on baseline predictor
$p^{(2)}$: significance p-value for interaction coefficient between time and baseline characteristic in a longitudinal regression model
$p^{(3)}$: p-value from Fisher's or Kruskal-Wallis test

Supplementary Table S13. Confounder selection for survival analysis.

Survival	Odds Ratio (95% CI)	p[(1)]	Between group difference, p[(3)]	Potential confounder	Retained
Age, years	1.0 (1.0 to 1.1)	0.003	0.324	Y	Y
Female, no.	1.2 (0.5 to 2.6)	0.697	0.003		
Months since onset of skin thickening	1.0 (0.9 to 1.0)	0.288	0.001		
Previous immunosuppressant use	1.6 (0.5 to 4.9)	0.428	0.007		
Current or previous steroid use	1.3 (0.6 to 2.7)	0.441	0.001		
mRSS	1.1 (1.0 to 1.1)	<0.0005	0.306	Y	Y
Haemoglobin g/l *	1.0 (0.9 to 1.0)	0.001	0.721	Y	
White blood count (WBC) x10^9/l *	1.0 (0.9 to 1.1)	0.882	0.029		
Platelets x10^9/l *	1.0 (1.0 to 1.0)	0.055	0.459		
ESR mm/hr *	1.0 (1.0 to 1.0)	0.012	0.341	Y	
CRP mg/l *	1.0 (1.0 to 1.1)	0.002	0.026	Y	
Anti-topoisomerase (anti-Scl70)	0.6 (0.3 to 1.3)	0.207	0.228		
Anti-RNA polymerase III	1.2 (0.5 to 3.3)	0.662	0.433		
Anticentromere	1.4 (0.4 to 4.9)	0.621	0.147		
Pulmonary fibrosis	2.7 (1.2 to 6.2)	0.015	0.036	Y	Y
FVC (% predicted) **	1.0 (1.0 to 1.0)	0.005	0.026	Y	
DLCO (% predicted) **	1.0 (1.0 to 1.0)	0.005	<0.0005	Y	
Pulmonary hypertension	4.5 (1.8 to 11.3)	0.001	0.488	Y	Y
sPAP or RVSP mmHg **	1.0 (1.0 to 1.1)	0.079	0.472		
Cardiac involvement	4.3 (1.9 to 9.6)	<0.0005	0.009	Y	Y
Renal involvement	1.6 (0.6 to 4.5)	0.351	0.039		Y
eGFR ml/min **	1.0 (1.0 to 1.0)	0.659	0.339		
Renal crisis **	1.2 (0.3 to 5.5)	0.815	0.110		
Plasma creatinine in µmol/l *	1.0 (1.0 to 1.0)	0.441	0.422		
Any GI involvement *	1.5 (0.7 to 3.0)	0.283	0.078		
Muscle involvement	1.3 (0.4 to 3.8)	0.683	0.002		
Current digital ulcers *	2.6 (1.2 to 5.6)	0.018	0.705	Y	
HAQ-DI Disability index (0-3)	2.4 (1.6 to 3.8)	<0.0001	0.400	Y	Y
FACIT fatigue score (0-52)	0.9 (0.9 to 1.0)	<0.0001	0.165	Y	Y
Cochin Hand Function Scale (0-90)	1.0 (1.0 to 1.0)	0.032	0.025	Y	Y

* Variable not considered as confounder due to lack of clinical significance or concerns about data completeness.
** Variable not considered as confounder because it was already an input in another aggregate variable (e.g. FVC in pulmonary fibrosis)

CRP: C-reactive protein
DLCO: Carbon monoxide diffusing capacity
ESR: Erythrocyte sedimentation rate
FVC: Forced vital capacity
GI: Gastrointestinal
HAQ-DI: Health Assessment Questionnaire - Disability Index
mRSS: modified Rodnan skin score (17 sites)
p[(1)]: significance p-value for odds ratio