

**Supplementary Table S1.** Comparison of clinical features between the MSAs (-), single MSAs (+) and multiple MSAs (+) groups in the overall population.

Characteristics	Total (N=202)	MSAs (-) (N=12)	Single MSAs (+) (N=146)	Multiple MSAs (+) (N=44)	p-value
<b>Demographics</b>					
Follow-up, months, (median [IQR])	22.50 [9.77, 44.75]	33.00 [17.25, 44.75]	20.50 [6.25, 44.75]	24.00 [11.75, 42.00]	0.421
Age, years, mean (S.D.)	48.86 (13.62)	45.00 (14.36)	48.95 (13.20)	49.61 (14.91)	0.578
Female gender, n (%)	119 (58.9)	8 (66.7)	89 (61.0)	22 (50.0)	0.371
Smoking, n (%)	40 (19.8)	2 (16.7)	26 (17.8)	12 (27.3)	0.359
<b>Clinical manifestations</b>					
Fever at presentation, n (%)	62 (30.7)	2 (16.7)	49 (33.6)	11 (25.0)	0.359
Rash, n (%)	140 (69.3)	5 (41.7)	103 (70.5)	32 (72.7)	0.113
Heliotrope rash, n (%)	85 (42.1)	5 (41.7)	63 (43.2)	17 (38.6)	0.936
Gottron papule/sign, n (%)	100 (49.5)	4 (33.3)	73 (50.0)	23 (52.3)	0.547
V-neck sign, n (%)	69 (34.2)	4 (33.3)	46 (31.5)	19 (43.2)	0.356
Periungual erythema, n (%)	30 (14.9)	0 (0.0)	27 (18.5)	3 (6.8)	0.067
Skin ulcers, n (%)	57 (28.2)	1 (8.3)	41 (28.1)	15 (34.1)	0.231
Mechanic's hands, n (%)	65 (32.2)	1 (8.3)	49 (33.6)	15 (34.1)	0.203
Raynaud phenomenon, n (%)	30 (14.9)	0 (0.0)	21 (14.4)	9 (20.5)	0.241
Dysphagia, n (%)	50 (24.8)	2 (16.7)	32 (21.9)	16 (36.4)	0.151
Hoarseness, n (%)	26 (12.9)	1 (8.3)	22 (15.1)	3 (6.8)	0.399
Peripheral oedema, n (%)	43 (21.3)	0 (0.0)	31 (21.2)	12 (27.3)	0.099
Articular symptom, n (%)	107 (53.0)	5 (41.7)	75 (51.4)	27 (61.4)	0.394
Cardiovascular involvement, n (%)	27 (13.4)	1 (8.3)	22 (15.1)	4 (9.1)	0.658
Serous effusion, n (%)	76 (37.6)	6 (50.0)	57 (39.0)	13 (29.5)	0.370
Muscle involvement, n (%)	147 (72.8)	10 (83.3)	103 (70.5)	34 (77.3)	0.567
Infection at presentation, n (%)	36 (17.8)	1 (8.3)	26 (17.8)	9 (20.5)	0.727
<b>ILD domain</b>					
ILD, n (%)	168 (83.2)	8 (66.7)	121 (82.9)	39 (88.6)	0.172
HRCT score, (median [IQR])	120.00 [104.97, 149.09]	126.98 [111.11, 143.92]	122.41 [105.11, 153.66]	114.00 [104.67, 136.16]	0.594
RP-ILD, n (%)	39 (19.3)	0 (0.0)	33 (22.6)	6 (13.6)	0.096
Lower lung zone consolidation, n (%)	69 (34.2)	4 (33.3)	48 (32.9)	17 (38.6)	0.756
HRCT pattern, n (%)					0.803
NSIP	38 (22.6)	1 (12.5)	28 (23.1)	9 (23.1)	
OP	71 (42.3)	4 (50.0)	48 (39.7)	19 (48.7)	
NSIP + OP	59 (35.1)	3 (37.5)	45 (37.2)	11 (28.2)	
<b>Laboratory features</b>					
WBC, ×10 <sup>9</sup> /l, mean (S.D.)	7.39 (3.75)	6.83 (2.49)	7.38 (3.42)	7.57 (4.97)	0.831
HB, g/L, mean (S.D.)	122.95 (19.39)	130.25 (13.49)	122.27 (20.15)	123.20 (18.04)	0.391
LY%, mean (S.D.)	19.83 (11.28)	18.63 (7.74)	19.36 (10.24)	21.70 (14.88)	0.452
NLR, (median [IQR])	3.99 [2.54, 6.60]	4.63 [2.50, 6.38]	3.99 [2.61, 6.60]	3.58 [2.34, 6.20]	0.797
CK level, U/L, (median [IQR])	223.50 [67.25, 2247.50]	192.00 [86.25, 1528.25]	261.50 [68.25, 2326.00]	207.50 [66.50, 895.75]	0.838
LDH, U/L, (median [IQR])	382.50 [263.75, 594.41]	272.50 [240.50, 509.50]	382.50 [267.25, 600.00]	428.50 [285.25, 613.25]	0.348
ALT, U/L, (median [IQR])	48.50 [21.00, 105.75]	33.00 [18.25, 68.25]	47.50 [22.00, 98.00]	54.50 [21.00, 151.00]	0.357
AST, U/L, (median [IQR])	58.00 [26.00, 127.75]	36.50 [25.00, 114.00]	59.50 [26.00, 127.00]	59.50 [28.00, 172.25]	0.748
ESR, mm/h, (median [IQR])	29.81 [14.25, 47.00]	21.17 [13.50, 39.75]	26.73 [14.25, 41.69]	34.31 [16.75, 55.50]	0.288
CRP, mg/L, (median [IQR])	5.31 [2.14, 16.00]	7.42 [4.67, 24.40]	4.96 [2.06, 15.42]	5.62 [2.12, 19.85]	0.496
Albumin, g/L, mean (S.D.)	34.41 (5.52)	35.26 (4.77)	34.15 (5.47)	35.07 (5.92)	0.537
ANA (≥1:80), n (%)	112 (55.4)	8 (67.7)	75 (51.4)	29 (65.9)	0.260
Anti-PM-SCL75, n (%)	11 (5.4)	1 (8.3)	8 (5.5)	2 (4.5)	0.769
Anti-SSA, n (%)	41 (20.3)	0 (0.0)	31 (21.2)	10 (22.7)	0.942
Anti-Ro52, n (%)	116 (57.4)	4 (33.3)	87 (59.6)	25 (56.8)	0.799
<b>Therapies</b>					
Exposure to high-dose glucocorticoid (≥80 mg), n (%)	90 (44.6)	5 (41.7)	67 (45.9)	18 (40.9)	0.851
No. of immunosuppressants, on top of steroid, n (%)					0.190
0	50 (24.8)	5 (41.7)	36 (24.7)	9 (20.5)	
1	103 (51.0)	7 (58.3)	71 (48.6)	25 (56.8)	
≥2	49 (24.3)	0 (0.0)	39 (26.7)	10 (22.7)	
IVIg, n (%)	65 (32.2)	4 (33.3)	48 (32.9)	13 (29.5)	0.931
Exposure to pirfenidone, n (%)	28 (13.9)	3 (25.0)	19 (13.0)	6 (13.6)	0.512

Bold indicates statistical significance.

MSAs: myositis-specific autoantibodies; ILD: interstitial lung disease; RP-ILD: rapidly progressive interstitial lung disease; HRCT: high-resolution computed tomography; NSIP: nonspecific interstitial pneumonia; OP: organising pneumonia; WBC: white blood cell count; HB: haemoglobin; LY%: percentage of lymphocyte; NLR: neutrophil/lymphocyte ratio; CK: creatine kinase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ANA: anti-nuclear antibody.

**Supplementary Table S2.** The prevalence of different MSAs in the multiple MSAs (+) group of anti-ARS+ population.

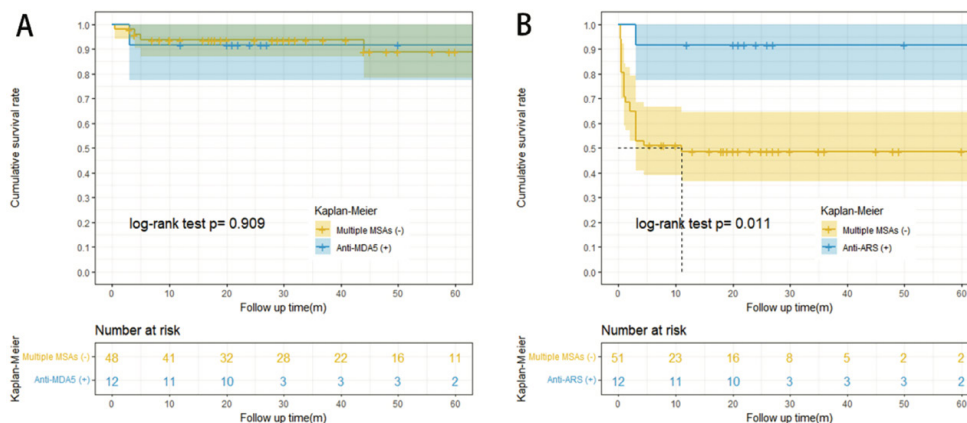
	Multiple MSAs (+) N=28
<b>Myositis-specific antibodies, n (%)</b>	
Anti-ARS	
Anti-Jo-1	12 (42.9)
Anti-OJ	2 (7.1)
Anti-PL7	7 (25.0)
Anti-PL12	9 (32.1)
Anti-EJ	1 (3.57)
Anti-SRP	5 (17.9)
Anti-MDA5	12 (42.9)
Anti-SAE	1 (3.57)
Anti-HMGCR	4 (14.3)
Anti-Mi-2	6 (21.4)
Anti-NXP2	5 (17.9)
Anti-TIF- $\gamma$	1 (3.6)

MSAs: myositis-specific autoantibodies; MDA5: melanoma differentiation-associated gene 5; TIF1- $\gamma$ : transcriptional intermediary factor 1 gamma; SAE: small ubiquitin-like modifier activating enzyme; NXP2: nuclear matrix protein 2; ARS: aminoacyl-tRNA synthetase; Jo-1: histidyl-tRNA-synthetase; PL-12: alanyl-tRNA synthetase; PL-7: threonyl-tRNA synthetase; EJ: glycyl-tRNA synthetase; OJ: isoleucyl-tRNA synthetase; HMGCR:3-hydroxy-3-methylglutaryl-coenzyme A reductase; SRP: signal recognition particle.

**Supplementary Table S3.** The prevalence of different MSAs in the multiple MSAs (+) group of anti-MDA5+ population.

	Multiple MSAs (+) N=23
<b>Myositis-specific antibodies, n (%)</b>	
Anti-ARS	12 (52.2)
Anti-Jo-1	5 (21.7)
Anti-OJ	2 (8.7)
Anti-PL7	4 (17.4)
Anti-PL12	2 (8.7)
Anti-EJ	1 (4.3)
Anti-SAE	2 (8.7)
Anti-SRP	5 (21.7)
Anti-Mi-2	7 (30.4)
Anti-NXP2	4 (17.4)
Anti-HMGCR	2 (8.7)
Anti-TIF- $\gamma$	2 (8.7)

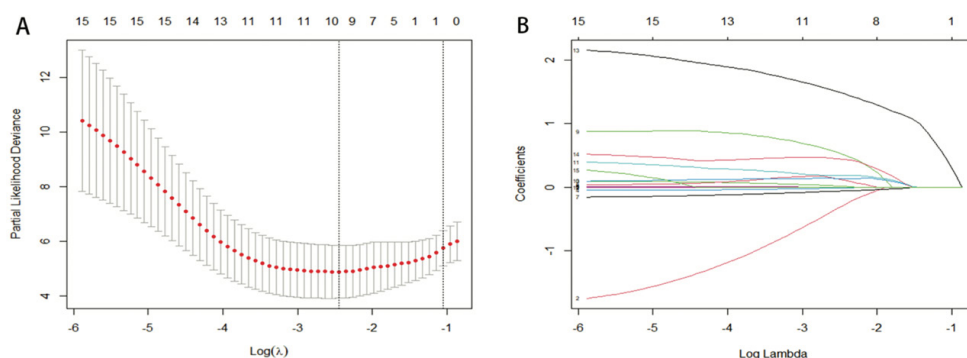
MSAs: myositis-specific autoantibodies; MDA5: melanoma differentiation-associated gene 5; TIF1- $\gamma$ : transcriptional intermediary factor 1 gamma; SAE: small ubiquitin-like modifier activating enzyme; NXP2: nuclear matrix protein 2; ARS: aminoacyl-tRNA synthetase; Jo-1: histidyl-tRNA-synthetase; PL-12: alanyl-tRNA synthetase; PL-7: threonyl-tRNA synthetase; EJ: glycyl-tRNA synthetase; OJ: isoleucyl-tRNA synthetase; HMGCR:3-hydroxy-3-methylglutaryl-coenzyme A reductase; SRP: signal recognition particle.



**Supplementary Fig. S1.** Kaplan-Meier survival curves for patients with and without multiple MSAs.

(A) The cumulative survival rate between anti-ARS+ population with coexisted anti-MDA5 antibody and those without multiple MSAs was similar (91.7% vs. 89.6%;  $p=0.909$ ). (B) The cumulative survival rate was significantly higher in anti-MDA5+ population with coexisted anti-ARS antibodies than those without multiple MSAs (91.7% vs. 49.0%;  $p=0.011$ ).

MSAs: myositis-specific autoantibodies; ARS: aminoacyl-tRNA synthetase; MDA5: melanoma differentiation-associated gene 5.



**Supplementary Fig. S2.** The most valuable predictors of mortality in anti-MDA5+ population were selected using LASSO Cox regression.

(A) Selection of the tuning parameter ( $\lambda$ ) in the LASSO Cox regression analysis using 10-fold cross-validation via minimum criteria in anti-MDA5+ population. (B) LASSO coefficient profiles of 15 candidate predictors.

**Supplementary Table S4.** Comparison of clinical features between anti- ARS+ population with coexisted anti-MDA5 antibody and those without multiple MSAs.

Characteristics	Total (N=60)	Multiple MSAs (-) (N=48)	Anti-MDA5 (+) (N=12)	p-value
<b>Demographics</b>				
Follow-up, months, (median [IQR])	30.50 [17.38, 56.00]	34.00 [17.00, 56.75]	24.00 [20.75, 32.75]	0.554
Age, years, mean (S.D.)	51.80 (11.12)	52.92 (11.24)	47.33 (9.80)	0.121
Female gender, n (%)	39 (65.0)	31 (64.6)	8 (66.7)	1.000
Smoking, n (%)	10 (16.7)	8 (16.7)	2 (16.7)	1.000
<b>Clinical manifestations</b>				
Fever at presentation, n (%)	18 (30.0)	15 (31.2)	3 (25.0)	1.000
Rash, n (%)	36 (60.0)	26 (54.2)	10 (83.3)	0.100
Heliotrope rash, n (%)	13 (21.7)	7 (14.6)	6 (50.0)	<b>0.015</b>
Gottron papule/sign, n (%)	21 (35.0)	15 (31.2)	6 (50.0)	0.312
V-neck sign, n (%)	11 (18.3)	5 (10.4)	6 (50.0)	<b>0.005</b>
Periungual erythema, n (%)	3 (5.0)	2 (4.2)	1 (8.3)	0.495
Skin ulcers, n (%)	8 (13.3)	3 (6.2)	5 (41.7)	<b>0.006</b>
Mechanic's hands, n (%)	25 (41.7)	21 (43.8)	4 (33.3)	0.745
Raynaud phenomenon, n (%)	11 (18.3)	10 (20.8)	1 (8.3)	0.435
Dysphagia, n (%)	6 (10.0)	4 (8.3)	2 (16.7)	0.590
Hoarseness, n (%)	4 (6.7)	2 (4.2)	2 (16.7)	0.175
Peripheral oedema, n (%)	7 (11.7)	4 (8.3)	3 (25.0)	0.135
Articular symptom, n (%)	39 (65.0)	31 (64.6)	8 (66.7)	1.000
Cardiovascular involvement, n (%)	6 (10.0)	6 (12.5)	0 (0.0)	0.333
Serous effusion, n (%)	27 (45.0)	23 (47.9)	4 (33.3)	0.519
Muscle involvement, n (%)	45 (75.0)	35 (72.9)	10 (83.3)	0.712
Infection at presentation, n (%)	6 (10.0)	4 (8.3)	2 (16.7)	0.590
<b>ILD domain</b>				
ILD, n (%)	58 (96.7)	46 (95.8)	12 (100.0)	1.000
HRCT score, (median [IQR])	125.75 [109.03, 161.52]	129.32 [113.22, 163.44]	108.48 [104.00, 130.16]	<b>0.025</b>
RP-ILD, n (%)	7 (11.7)	5 (10.4)	2 (16.7)	0.619
Lower lung zone consolidation, n (%)	23 (38.3)	18 (37.5)	5 (41.7)	1.000
HRCT patterns, n (%)		0.115		
NSIP	14 (24.1)	12 (26.1)	2 (16.7)	
OP	23 (39.7)	15 (32.6)	8 (66.7)	
NSIP + OP	21 (36.2)	19 (41.3)	2 (16.7)	
<b>Laboratory features</b>				
WBC, ×10 <sup>9</sup> /l, mean (S.D.)	8.38 (3.93)	9.08 (3.96)	5.60 (2.33)	<b>0.005</b>
HB, g/L, mean (S.D.)	128.08 (16.38)	128.98 (15.74)	124.50 (19.07)	0.402
LY%, mean (S.D.)	20.07 (9.30)	20.08 (9.86)	20.07 (6.96)	0.998
NLR, (median [IQR])	3.71 [2.50, 5.94]	3.84 [2.44, 6.02]	3.11 [2.71, 5.20]	0.767
CK level, U/L, (median [IQR])	261.50 [66.50, 1688.11]	297.00 [72.75, 2164.25]	105.50 [54.25, 430.75]	0.106
LDH, U/L, (median [IQR])	22.50 [12.00, 34.72]	22.00 [11.75, 34.25]	26.01 [16.75, 40.97]	0.405
ALT, U/L, (median [IQR])	32.00 [14.75, 77.85]	30.03 [14.75, 81.25]	32.00 [19.00, 53.25]	0.963
AST, U/L, (median [IQR])	32.50 [21.62, 85.25]	30.35 [19.00, 95.50]	38.00 [28.00, 57.25]	0.309
ESR, mm/h, (median [IQR])	316.00 [230.50, 477.58]	303.50 [228.50, 483.00]	331.00 [235.50, 440.00]	0.839
CRP, mg/L, (median [IQR])	25.00 [13.75, 62.25]	25.00 [13.75, 72.25]	25.50 [18.75, 43.75]	0.698
Albumin, g/L, mean (S.D.)	35.24 (5.26)	35.34 (5.10)	34.84 (6.08)	0.772
ANA (≥1:80), n (%)	44 (73.3)	35 (72.9)	9 (75.0)	1.000
Anti-PM-SCL75, n (%)	3 (5.0)	3 (6.3)	0 (0.0)	1.000
Anti-SSA, n (%)	20 (33.3)	17 (35.4)	3 (25.0)	0.732
Anti-Ro52, n (%)	45 (75.0)	36 (75.0)	9 (75.0)	1.000
<b>Therapies</b>				
Exposure to high-dose glucocorticoid (≥80 mg), n (%)	18 (30.0)	11 (22.9)	7 (58.3)	<b>0.031</b>
No. of immunosuppressants, on top of steroid, n (%)				0.350
0	12 (20.0)	11 (22.9)	1 (8.3)	
1	32 (53.3)	26 (54.2)	6 (50.0)	
≥2	16 (26.7)	11 (22.9)	5 (41.7)	
IVIg, n (%)	16 (26.7)	12 (25.0)	4 (33.3)	0.716
Exposure to pirfenidone, n (%)	18 (30.0)	13 (27.1)	5 (41.7)	0.482

Bold indicates statistical significance.

MSAs: myositis-specific autoantibodies; ARS: aminoacyl-tRNA synthetase; MDA5: melanoma differentiation-associated gene 5; ILD: interstitial lung disease; RP-ILD: rapidly progressive interstitial lung disease; HRCT: high-resolution computed tomography. NSIP: nonspecific interstitial pneumonia; OP: organising pneumonia; WBC: white blood cell count; HB: haemoglobin; LY%: percentage of lymphocyte; NLR: neutrophil/lymphocyte ratio; CK: creatine kinase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ANA: anti-nuclear antibody.

**Supplementary Table S5.** Comparison of clinical features between anti-MDA5+ population with coexisted anti-ARS antibodies and those without multiple MSAs.

Characteristics	Total (N=63)	Multiple MSAs (-) (N=51)	Anti-ARS (+) (N=12)	p-value
<b>Demographics</b>				
Follow-up, months, (median [IQR])	13.00 [1.60, 26.00]	7.60 [1.00, 24.00]	24.00 [20.75, 32.75]	<b>0.006</b>
Age, years, mean (S.D.)	47.22 (13.05)	47.20 (13.79)	47.33 (9.80)	0.974
Female gender, n (%)	38 (60.3)	30 (58.8)	8 (66.7)	0.749
Smoking, n (%)	12 (19.0)	10 (19.6)	2 (16.7)	1.000
<b>Clinical manifestations</b>				
Fever at presentation, n (%)	30 (47.6)	27 (52.9)	3 (25.0)	0.112
Rash, n (%)	60 (95.2)	50 (98.0)	10 (83.3)	0.090
Heliotrope rash, n (%)	41 (65.1)	35 (68.6)	6 (50.0)	0.314
Gottron papule/sign, n (%)	50 (79.4)	44 (86.3)	6 (50.0)	<b>0.012</b>
V-neck sign, n (%)	36 (57.1)	30 (58.8)	6 (50.0)	0.747
Periungual erythema, n (%)	21 (33.3)	20 (39.2)	1 (8.3)	<b>0.048</b>
Skin ulcers, n (%)	33 (52.4)	28 (54.9)	5 (41.7)	0.525
Mechanic's hands, n (%)	21 (33.3)	17 (33.3)	4 (33.3)	1.000
Raynaud phenomenon, n (%)	6 (9.5)	5 (9.8)	1 (8.3)	1.000
Dysphagia, n (%)	8 (12.7)	6 (11.8)	2 (16.7)	0.641
Hoarseness, n (%)	10 (15.9)	8 (15.7)	2 (16.7)	1.000
Peripheral oedema, n (%)	13 (20.6)	10 (19.6)	3 (25.0)	0.700
Articular symptom, n (%)	38 (60.3)	30 (58.8)	8 (66.7)	0.749
Cardiovascular involvement, n (%)	9 (14.3)	9 (17.6)	0 (0.0)	0.187
Serous effusion, n (%)	28 (44.4)	24 (47.1)	4 (33.3)	0.523
Muscle involvement, n (%)	36 (57.1)	26 (51.0)	10 (83.3)	0.055
Infection at presentation, n (%)	19 (30.2)	17 (33.3)	2 (16.7)	0.318
<b>ILD domain</b>				
ILD, n (%)	62 (98.4)	50 (98.0)	12 (100.0)	1.000
HRCT score, (median [IQR])	126.33 [104.77, 153.17]	127.70 [105.94, 158.64]	108.48 [104.00, 130.16]	0.167
RP-ILD, n (%)	30 (47.6)	28 (54.9)	2 (16.7)	<b>0.024</b>
Lower lung zone consolidation, n (%)	30 (47.6)	25 (49.0)	5 (41.7)	0.754
HRCT patterns, n (%)				0.236
NSIP	6 (9.7)	4 (8.0)	2 (16.7)	
OP	34 (54.8)	26 (52.0)	8 (66.7)	
NSIP + OP	22 (35.5)	20 (40.0)	2 (16.7)	
<b>Laboratory features</b>				
WBC, ×10 <sup>9</sup> /l, mean (S.D.)	5.59 (2.00)	5.59 (1.93)	5.60 (2.33)	0.983
HB, g/L, mean (S.D.)	117.02 (20.60)	115.25 (20.73)	124.50 (19.07)	0.164
LY%, mean (S.D.)	16.70 (6.52)	15.90 (6.22)	20.07 (6.96)	<b>0.046</b>
NLR, (median [IQR])	4.46 [2.92, 6.68]	4.64 [3.17, 6.87]	3.11 [2.71, 5.20]	0.083
CK level, U/L, (median [IQR])	80.00 [46.50, 264.00]	80.00 [46.50, 200.50]	105.50 [54.25, 430.75]	0.593
LDH, U/L, (median [IQR])	32.00 [20.50, 57.00]	34.00 [22.00, 57.00]	26.01 [16.75, 40.97]	0.234
ALT, U/L, (median [IQR])	42.00 [22.50, 71.50]	46.00 [23.50, 72.00]	32.00 [19.00, 53.25]	0.327
AST, U/L, (median [IQR])	54.00 [33.50, 88.50]	61.00 [43.00, 94.00]	38.00 [28.00, 57.25]	0.149
ESR, mm/h, (median [IQR])	355.00 [289.06, 559.50]	369.00 [295.56, 581.50]	331.00 [235.50, 440.00]	0.286
CRP, mg/L, (median [IQR])	17.00 [13.00, 25.00]	16.00 [13.00, 23.00]	25.50 [18.75, 43.75]	<b>0.039</b>
Albumin, g/L, mean (S.D.)	32.20 (5.78)	31.58 (5.58)	34.84 (6.08)	0.078
ANA (≥1:80), n (%)	22 (34.9)	13 (25.5)	9 (75.0)	<b>0.002</b>
Anti-PM-SCL75, n (%)	2 (3.2)	2 (3.9)	0 (0.0)	1.000
Anti-SSA, n (%)	11 (17.5)	8 (15.7)	3 (25.0)	0.732
Anti-Ro52, n (%)	48 (76.2)	39 (76.5)	9 (75.0)	1.000
<b>Therapies</b>				
Exposure to high-dose glucocorticoid (≥80 mg), n (%)	37 (58.7)	30 (58.8)	7 (58.3)	1.000
No. of immunosuppressants, on top of steroid, n (%)				0.547
0	13 (20.6)	12 (23.5)	1 (8.3)	
1	24 (38.1)	18 (35.3)	6 (50.0)	
≥2	26 (41.3)	21 (41.2)	5 (41.7)	
IVIg, n (%)	26 (41.3)	21 (41.2)	5 (41.7)	1.000
Exposure to pirfenidone, n (%)	9 (14.3)	5 (9.8)	4 (33.3)	0.058

Bold indicates statistical significance.

MSAs: myositis-specific autoantibodies; ARS: aminoacyl-tRNA synthetase; MDA5: melanoma differentiation-associated gene 5; ILD: interstitial lung disease; RP-ILD: rapidly progressive interstitial lung disease; HRCT: high-resolution computed tomography. NSIP: nonspecific interstitial pneumonia; OP: organising pneumonia; WBC: white blood cell count; HB: haemoglobin; LY%: percentage of lymphocyte; NLR: neutrophil/lymphocyte ratio; CK: creatine kinase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ANA: anti-nuclear antibody.

Supplementary Table S6. Clinical features of anti-MDA5+ population with non-survivors and predictors of mortality.

Characteristics	Survivors (N=45)	Non-survivors (N=29)	p-value	Univariate Cox regression analysis HR (95% CI)	p-value
<b>Demographics</b>					
Follow-up, months, (median [IQR])	24.00 [18.00, 36.00]	1.00 [0.50, 3.00]	<b>&lt;0.001</b>		
Age, years, mean (S.D.)	43.87 (13.42)	52.38 (11.93)	<b>0.007</b>	1.039 (1.008-1.071)	<b>0.015</b>
Female gender, n (%)	30 (66.7)	13 (44.8)	0.091		
Smoking, n (%)	6 (13.3)	9 (31.0)	0.080		
<b>Clinical manifestations</b>					
Fever at presentation, n (%)	13 (28.9)	19 (65.5)	<b>0.004</b>	3.800 (1.760-8.206)	<b>0.001</b>
Rash, n (%)	41 (91.1)	28 (96.6)	0.642		
Heliotrope rash, n (%)	29 (64.4)	20 (69.0)	0.803		
Gottron papule/sign, n (%)	36 (80.0)	23 (79.3)	1.000		
V-neck sign, n (%)	23 (51.1)	19 (65.5)	0.241		
Periungual erythema, n (%)	14 (31.1)	9 (31.0)	1.000		
Skin ulcers, n (%)	21 (46.7)	18 (62.1)	0.237		
Mechanic's hands, n (%)	18 (40.0)	9 (31.0)	0.469		
Raynaud phenomenon, n (%)	9 (20.0)	1 (3.4)	0.078		
Dysphagia, n (%)	10 (22.2)	4 (13.8)	0.545		
Hoarseness, n (%)	9 (20.0)	2 (6.9)	0.183		
Peripheral oedema, n (%)	9 (20.0)	5 (17.2)	1.000		
Articular symptom, n (%)	32 (71.1)	14 (48.3)	0.055		
Cardiovascular involvement, n (%)	3 (6.7)	7 (24.1)	<b>0.042</b>	3.330 (1.412-7.857)	<b>0.006</b>
Serous effusion, n (%)	10 (22.2)	20 (69.0)	<b>&lt;0.001</b>	4.853 (2.199-10.713)	<b>&lt;0.001</b>
Muscle involvement, n (%)	27 (60.0)	17 (58.6)	1.000		
Infection at presentation, n (%)	4 (8.9)	16 (55.2)	<b>&lt;0.001</b>	5.627 (2.676-11.836)	<b>&lt;0.001</b>
<b>ILD domain</b>					
ILD, n (%)	44 (97.8)	29 (100.0)	1.000		
HRCT score, (median [IQR])	109.00 [103.69, 136.50]	146.50 [126.33, 171.00]	<b>&lt;0.001</b>	1.010 (1.004-1.015)	<b>0.001</b>
RP-ILD, n (%)	8 (17.8)	25 (86.2)	<b>&lt;0.001</b>	15.705 (5.385-45.805)	<b>&lt;0.001</b>
Lower lung zone consolidation, n (%)	19 (42.2)	16 (55.2)	0.343		
HRCT patterns, n (%)			0.155		
NSIP	7 (15.9)	1 (3.4)			
OP	24 (54.5)	15 (51.7)			
NSIP + OP	13 (29.5)	13 (44.8)			
<b>Laboratory features</b>					
WBC, ×10 <sup>9</sup> /l, mean (S.D.)	5.24 (1.91)	6.70 (3.57)	<b>0.026</b>	1.111 (1.012-1.219)	<b>0.027</b>
HB, g/L, mean (S.D.)	119.64 (18.88)	115.14 (20.95)	0.340		
LY%, mean (S.D.)	18.99 (10.29)	13.83 (6.26)	<b>0.018</b>	0.939 (0.892-0.987)	<b>0.014</b>
NLR, (median [IQR])	3.55 [2.75, 6.05]	5.14 [4.24, 7.11]	<b>0.013</b>	0.998 (0.970-1.027)	0.890
CK level, U/L, (median [IQR])	77.00 [45.00, 344.00]	135.00 [56.00, 374.00]	0.445		
LDH, U/L, (median [IQR])	339.00 [278.00, 458.00]	399.00 [312.00, 670.00]	0.082		
ALT, U/L, (median [IQR])	41.00 [21.00, 105.00]	46.00 [31.00, 72.00]	0.492		
AST, U/L, (median [IQR])	45.00 [28.00, 83.00]	69.00 [49.00, 117.00]	<b>0.021</b>	1.001 (1.000-1.001)	0.123
ESR, mm/h, (median [IQR])	30.01 [20.00, 40.00]	42.00 [26.00, 80.53]	<b>0.010</b>	1.014 (1.005-1.023)	<b>0.001</b>
CRP, mg/L, (median [IQR])	4.89 [2.23, 9.77]	14.20 [6.29, 26.60]	<b>0.003</b>	1.018 (1.004-1.032)	<b>0.011</b>
Albumin, g/L, mean (S.D.)	34.79 (5.44)	28.80 (3.44)	<b>&lt;0.001</b>	0.842 (0.780-0.909)	<b>&lt;0.001</b>
ANA (≥1:80), n (%)	17 (37.8)	11 (37.9)	1.000		
Anti-PM-SCL75, n (%)	2 (4.4)	0 (0.0)	0.517		
Anti-SSA, n (%)	8 (17.8)	4 (13.8)	0.896		
Anti-Ro52, n (%)	30 (66.7)	25 (86.2)	0.060		
Multiple MSAs, n (%)	20 (44.4)	3 (10.3)	<b>0.002</b>	0.193 (0.058-0.637)	<b>0.007</b>
<b>Myositis-specific antibodies, n (%)</b>					
Anti-Mi2, n (%)	7 (15.6)	0 (0.0)	<b>0.038</b>	0.041 (0.000-6.083)	0.211
Anti-TIF- $\gamma$ , n (%)	2 (4.4)	0 (0.0)	0.517		
Anti-NXP2, n (%)	3 (6.7)	1 (3.4)	1.000		
Anti-ARS, n (%)	11 (24.4)	1 (3.4)	<b>0.022</b>	0.141 (0.019-1.035)	0.054
Anti-Jo1, n (%)	5 (11.1)	0 (0.0)	0.150		
Anti-PL7, n (%)	5 (11.1)	0 (0.0)	0.150		
Anti-PL12, n (%)	1 (2.2)	1 (3.4)	1.000		
Anti-EJ, n (%)	1 (2.2)	0 (0.0)	1.000		
Anti-OJ, n (%)	2 (4.4)	0 (0.0)	0.517		
Anti-SAE, n (%)	0 (0.0)	0 (0.0)	NA		
Anti-SRP, n (%)	4 (8.9)	1 (3.4)	0.642		
Anti-HMGCR, n (%)	2 (4.4)	0 (0.0)	0.517		
<b>Therapies</b>					
Exposure to high-dose glucocorticoid (≥80 mg), n (%)	21 (46.7)	18 (62.1)	0.237		
No. of immunosuppressants, on top of steroid, n (%)					
0	4 (8.9)	12 (41.4)	<b>0.001</b>	4.060 (1.924-8.564)	<b>&lt;0.001</b>
1	19 (42.2)	11 (37.9)	0.714		
≥2	22 (48.9)	6 (20.7)	<b>0.015</b>	0.330 (0.134-0.813)	<b>0.016</b>
IVIg, n (%)	13 (28.9)	14 (48.3)	0.137		
Exposure to pirfenidone, n (%)	9 (20.0)	0 (0.0)	<b>0.010</b>	0.039 (0.000-3.383)	0.154

Bold indicates statistical significance.

MSAs: myositis-specific autoantibodies; MDA5: melanoma differentiation-associated gene 5; TIF1- $\gamma$ : transcriptional intermediary factor 1 gamma; SAE: small ubiquitin-like modifier activating enzyme; NXP2: nuclear matrix protein 2; ARS: aminoacyl-tRNA synthetase; Jo-1: histidyl-tRNA-synthetase; PL-12: alanyl-tRNA synthetase; PL-7: threonyl-tRNA synthetase; EJ: glycyl-tRNA synthetase; OJ: isoleucyl-tRNA synthetase; HMGCR:3-hydroxy-3-methylglutaryl-coenzyme A reductase; SRP: signal recognition particle; ILD: interstitial lung disease; RP-ILD: rapidly progressive interstitial lung disease; HRCT: high-resolution computed tomography. NSIP: nonspecific interstitial pneumonia; OP: organising pneumonia; WBC: white blood cell count; HB: haemoglobin; LY%: percentage of lymphocyte; NLR: neutrophil/lymphocyte ratio; CK: creatine kinase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ANA: anti-nuclear antibody.