

Supplemental Material

Table 1 Supplemental. Demographic, clinical and laboratory features at IIM diagnosis in the overall IIMs population and in patients categorized as not associated with ILD (non-ILD), with ILD at baseline or during follow-up (ILD at FU).

	Overall IIMs population (n=253)	IIMs non-ILD (n=128)	ILD at baseline (n=99)	ILD at FU (n = 26)	IIMs non-ILD Vs. ILD at baseline <i>p value</i>	ILD at baseline vs. ILD at FU <i>p value</i>	IIMs non-ILD vs. ILD at FU <i>p value</i>
<i>Demographics</i>							
Female - <i>n (%)</i>	183 (72)	94 (73)	71 (72)	18 (69)	0.77	0.92	0.66
Age at diagnosis - <i>yr</i>	55 (46 - 66)	54 (41 - 67)	57 (50 - 67)	54 (48 - 60)	0.02	0.10	0.91
Follow-up duration - <i>yr</i>	6 (3 - 10)	6 (3 - 10)	5 (2 -8)	6 (4.5 -10)	0.14	0.01	0.19
History of cancer – <i>n (%)</i>	37 (15)	20 (16)	14 (14)	3 (12)	0.76	0.73	0.59
<i>IIM phenotype</i>							
Polymyositis – <i>n (%)</i>	67 (27)	41 (32)	19 (19)	7 (27)	0.03	0.38	0.60
Dermatomyositis – <i>n (%)</i>	96 (38)	67 (52)	21 (21)	8 (31)	<0.0001	0.30	0.04
Inclusion body myositis – <i>n (%)</i>	5 (2)	5 (4)	0 (0)	0 (0)	0.04	n.a.	0.31
Necrotizing autoimmune myopathy – <i>n (%)</i>	8 (3)	8 (6)	0 (0)	0 (0)	0.01	n.a.	0.19
Anti-synthetase Syndrome – <i>n (%)</i>	77 (30)	7 (5)	59 (60)	11 (42)	<0.0001	0.11	<0.0001
<i>Muscle involvement</i>							

Muscle biopsy - <i>n</i> (%)	108 (43)	70 (55)	28 (28)	10 (38)	<0.0001	0.31	0.13
Muscle biopsy abnormalities - <i>n</i> (%)	95 (38)	62 (48)	24 (24)	9 (35)	0.0002	0.18	0.32
Muscle MRI - <i>n</i> (%)	109 (43)	65 (51)	35 (35)	9 (35)	0.02	0.94	0.13
MRI abnormalities - <i>n</i> (%)	96 (40)	63 (49)	24 (24)	9 (35)	<0.0001	0.28	0.17
Myositis (biopsy and/or MRI) - <i>n</i> (%)	155 (61)	97 (76)	44 (44)	14 (54)	<0.0001	0.39	0.02
CK at diagnosis - U/L	674 (128 - 3268)	1,264 (168 - 5,007)	514 (100 - 3,000)	160 (100 - 1,418)	0.007	0.09	0.002
MMT-8 at diagnosis	140 (120-150)	133.5 (112-148)	145 (126 - 150)	150 (140 - 150)	0.0004	0.02	<0.0001
<i>Clinical features</i>							
Arthralgia - <i>n</i> (%)	128 (51)	53 (41)	58 (59)	17 (65)	0.01	0.52	0.02
Arthritis - <i>n</i> (%)	53 (21)	15 (12)	32 (32)	6 (23)	<0.0001	0.36	0.12
Muscle weakness - <i>n</i> (%)	171 (68)	99 (77)	61 (62)	11 (42)	0.01	0.07	0.0003
Fever - <i>n</i> (%)	48 (19)	15 (12)	26 (26)	7 (27)	0.005	0.86	0.03
Fatigue- <i>n</i> (%)	119 (47)	60 (47)	47 (47)	13 (50)	0.92	0.65	0.77
Heliotropic rash - <i>n</i> (%)	74 (29)	56 (44)	14 (14)	4 (15)	< 0.0001	0.87	0.007
Gottron's papules - <i>n</i> (%)	40 (16)	23 (18)	14 (14)	3 (12)	0.42	0.59	0.46
Gottron's sign - <i>n</i> (%)	37 (15)	24 (19)	11 (11)	2 (7)	0.11	0.66	0.17
Mechanic's hands - <i>n</i> (%)	30 (12)	4 (3)	20 (20)	6 (23)	< 0.0001	0.74	0.0002
Raynaud's phenomenon - <i>n</i> (%)	47 (19)	16 (13)	23 (23)	8 (31)	0.03	0.42	0.01

Dysphonia - n (%)	9 (4)	3 (2)	4 (4)	2 (7)	0.47	0.43	0.10
Dysphagia - n (%)	58 (23)	42 (33)	13 (13)	3 (12)	<0.0001	0.68	0.001
Xerostomia - n (%)	23 (9)	9 (7)	11 (11)	3 (12)	0.29	0.95	0.43
Xerophthalmia - n (%)	21 (8)	8 (6)	9 (9)	4 (16)	0.42	0.34	0.11
Dyspnoea - n (%)	68 (27)	8 (6)	50 (51)	10 (38)	<0.0001	0.34	<0.0001
Cough - n (%)	26 (10)	2 (1)	21 (21)	3 (12)	<0.0001	0.40	0.007
Autoantibody profile							
Myositis-specific antibodies - n (%)	162 (64)	51 (40)	71 (72)	16 (62)	<0.0001	0.31	0.04
Myositis-associated antibodies - n (%)	138 (55)	47 (36)	57 (58)	16 (62)	0.002	0.71	0.02
Anti-synthetase - n (%)	120 (47)	12 (9)	60 (61)	15 (58)	<0.0001	0.8	<0.0001
Antinuclear antibodies - n (%)	87 (34)	74 (58)	70 (71)	18 (69)	0.04	0.88	0.27
Anti-Jo-1 - n (%)	63 (25)	7 (5)	43 (43)	13 (50)	<0.0001	0.54	<0.0001
Anti-PL12 - n (%)	13 (5)	4 (3)	8 (8)	1 (38)	0.09	0.45	0.85
Anti-PL7 - n (%)	14 (6)	6 (5)	6 (6)	2 (7)	0.65	0.76	0.52
Anti-PM/Scl - n (%)	29 (11)	12 (9)	13 (13)	4 (15)	0.39	0.76	0.37
Anti-SSA/Ro - n (%)	80 (32)	23 (18)	45 (45)	12 (46)	<0.0001	0.94	0.002
Anti-SSB/La - n (%)	10 (4)	6 (5)	3 (3)	1 (4)	0.52	0.83	0.85
Anti-U1RNP - n (%)	9 (3)	6 (5)	3 (3)	0 (0)	0.52	0.36	0.26
Anti-Ku - n (%)	21 (8)	4 (3)	1 (1)	4 (15)	0.28	0.0009	0.01

Anti-TIF1 γ - n (%)	9 (3)	6 (5)	1 (1)	0 (0)	0.11	0.61	0.26
Anti-Ro52 - n (%)	7 (3)	11 (8)	37 (37)	6 (23)	<0.0001	0.17	0.03
Anti-MDA5 - n (%)	10 (4)	1 (1)	8 (8)	1 (4)	0.005	0.45	0.20
Anti-EJ - n (%)	10 (4)	1 (1)	3 (3)	0 (0)	0.20	0.37	0.65
Anti-SRP - n (%)	4 (1.5)	12 (9)	3 (3)	1 (4)	0.05	0.83	0.36
Anti-Mi2 - n (%)	16 (6)	17 (13)	4 (4)	0 (0)	0.01	0.30	0.04
Anti-SAE1 - n (%)	3 (1)	3 (2)	0 (0)	0 (0)	0.12	n.a.	0.43

Values are expressed as numbers and (%) or median and ranges, as appropriate. ANA, anti-nuclear antibodies; CK, creatine kinase; ENA, extractable nuclear antigen; FU, follow-up; ILD, interstitial lung disease; KCO, carbon monoxide transfer coefficient; MDA5, anti-melanoma differentiation-associated gene; MMT, manual muscle test; MRI, magnetic resonance imaging; RNP, ribonucleoprotein; SAE, small ubiquitin-like modifier-1 activating enzyme; SRP, signal recognition particle; TIF1 γ , transcription intermediary factor 1-gamma

Table 2 Supplemental. Clinical, serological and functional characteristics at IIMs-ILD diagnosis in the sub-grouped IIM-ILD population at IIMs-ILD diagnosis, categorized according to the predominant radiographic pattern.

	Total population n=78	NSIP n=39	UIP n=22	OP n=17	p value
<i>Demographics</i>					
Male - <i>n (%)</i>	23 (29)	12 (31)	6 (27)	5 (29)	0.96
Female - <i>n (%)</i>	55 (71)	27 (69)	16 (73)	12 (71)	
Age at myositis diagnosis - <i>years</i>	57 (50-66)	57 (51-64)	58 (48-70)	57 (50-62)	0.90
Age at ILD diagnosis - <i>years</i>	57 (50-66)	57 (51-64)	60 (49-69)	57 (50-62)	0.70
Lag time symptoms-diagnosis - <i>years</i>	0 (0-1)	0.5 (0-1)	0 (0-1)	0 (0-1)	0.17
Time from myositis diagnosis to ILD - <i>years</i>	0 (-8 - 24)	0 (-1-24)	0 (-5-13)	0 (-8-0)	0.04
Follow-up duration - <i>years</i>	4 (2-6)	5 (3-7)	5.5 (3-7)	3 (2-3)	0.055
Deaths - <i>n (%)</i>	1 (1)	0 (0)	1 (5)	0 (0)	-
<i>IIMs phenotype</i>					
Polymyositis - <i>n (%)</i>	17 (22)	9 (23)	6 (27)	2 (12)	0.34
Dermatomyositis - <i>n (%)</i>	20 (26)	13 (33)	3 (14)	4 (24)	
Anti-synthetase Syndrome - <i>n (%)</i>	41 (53)	17 (44)	13 (59)	11 (65)	
<i>Clinical features</i>					

Myalgia - <i>n</i> (%)	40 (51)	24 (62)	4 (18)	12 (71)	0.001
Muscle Weakness - <i>n</i> (%)	47 (59)	25 (64)	9 (41)	13 (76)	0.06
Asthenia - <i>n</i> (%)	39 (49)	21 (54)	6 (27)	12 (71)	0.02
Dyspnea - <i>n</i> (%)	36 (46)	17 (44)	9 (41)	10 (59)	0.49
Cough - <i>n</i> (%)	19 (24)	8 (21)	6 (27)	5 (29)	0.72
Dysphonia - <i>n</i> (%)	4 (5)	2 (5)	2 (9)	0 (0)	0.66
Dysphagia - <i>n</i> (%)	12 (15)	4 (10)	5 (23)	3 (18)	0.39
Fever - <i>n</i> (%)	21 (27)	10 (26)	5 (23)	6 (35)	0.66
Arthralgia - <i>n</i> (%)	45 (57)	24 (62)	12 (55)	9 (53)	0.79
Arthritis - <i>n</i> (%)	26 (33)	18 (46)	4 (18)	4 (24)	0.006
Mechanic's hands - <i>n</i> (%)	19 (24)	9 (23)	4 (18)	6 (35)	0.45
Heliotropic rash - <i>n</i> (%)	15 (19)	7 (18)	4 (18)	4 (24)	0.87
Raynaud's phenomenon - <i>n</i> (%)	19 (24)	10 (26)	5 (23)	4 (24)	1.00
Gottron's sign - <i>n</i> (%)	10 (13)	5 (13)	2 (9)	3 (18)	0.82
Gottron's papules - <i>n</i> (%)	10 (13)	5 (13)	1 (5)	4 (24)	0.22
Calcinosis - <i>n</i> (%)	2 (3)	1 (3)	0 (0)	1 (6)	0.47
Xerophthalmia - <i>n</i> (%)	12 (15)	6 (15)	2 (9)	4 (24)	0.47
Xerostomia - <i>n</i> (%)	9 (11)	5 (13)	1 (5)	3 (18)	0.37
<i>Muscle involvement</i>					

CK- U/L	567 (100-2117)	525 (139-2005)	121 (80-672)	1380 (157-3339)	0.04
MMT-8	145 (122-150)	145 (134-150)	150 (135-150)	120 (105-146)	0.005
Myositis (biopsy and/or MRI) - <i>n</i> (%)	42 (54)	19 (49)	11 (50)	12 (71)	0.29
<i>Autoantibody profile</i>					
Myositis-specific antibodies - <i>n</i> (%)	54 (69)	27 (69)	14 (63)	13 (76)	0.69
Myositis-associated antibodies - <i>n</i> (%)	47 (60)	21 (54)	14 (63)	12 (71)	0.46
Anti-synthetase - <i>n</i> (%)	40 (51)	21 (54)	9 (41)	10 (59)	0.49
Anti-ENA - <i>n</i> (%)	51 (65)	23 (59)	15 (68)	13 (76)	0.43
ANA - <i>n</i> (%)	53 (68)	28 (72)	13 (59)	12 (71)	0.57
Anti-Jo1 - <i>n</i> (%)	32 (41)	14 (36)	9 (41)	9 (53)	0.49
Anti-PL12 - <i>n</i> (%)	6 (8)	2 (5)	4 (18)	0 (0)	0.09
Anti-PL7 - <i>n</i> (%)	6 (8)	4 (10)	1 (5)	1 (6)	0.86
Anti-Pm/Scl - <i>n</i> (%)	12 (15)	6 (15)	4 (18)	2 (12)	0.92
Anti-SSA - <i>n</i> (%)	32 (41)	15 (38)	7 (32)	10 (59)	0.21
Anti-SSB - <i>n</i> (%)	2 (2)	0 (0)	0 (0)	2 (12)	0.04
Anti-U1RNP - <i>n</i> (%)	2 (2)	1 (3)	0 (0)	1 (6)	0.46
Anti-Ku - <i>n</i> (%)	3 (4)	3 (8)	0 (0)	0 (0)	0.30

Anti-TIF1G - <i>n</i> (%)	1 (1)	1 (3)	0 (0)	0 (0)	1.00
Anti-Ro52 - <i>n</i> (%)	28 (36)	11 (28)	7 (32)	10 (59)	0.08
Anti-MDA5 - <i>n</i> (%)	7 (9)	4 (10)	0 (0)	3 (18)	0.13
Anti-EJ - <i>n</i> (%)	1 (1)	1 (3)	0 (0)	0 (0)	1.00
Anti-SRP - <i>n</i> (%)	2 (2)	1 (3)	1 (5)	0 (0)	1.00
Anti-MI2 - <i>n</i> (%)	3 (4)	3 (8)	0 (0)	0 (0)	0.30
<i>Pulmonary function tests</i>					
FVC - L	2.56 (2.16-3.21)	2.92 (2.44-3.23)	2.56 (1.7-2.83)	2.38 (2.18-2.67)	0.08
FVC - % pred.	84 (70-94)	89 (80-111)	74 (60-92)	72 (58-88)	0.003
TLC – L	4.43 (3.56-4.97)	4.58 (3.89-5.55)	4.17 (3.25-4.79)	4.59 (3.54-4.68)	0.45
TLC - % pred.	81 (65-90)	85 (71-99)	75 (61-89)	82 (69-86)	0.13
DLCO - % pred.	58 (42-69)	58 (46-77)	49 (40-66)	58 (45-66)	0.41
KCO - % pred.	81 (64-90)	78 (61-94)	78 (62-85)	86 (74-88)	0.74
Immunosuppressants <i>n</i> - %	41 (53)	20 (51)	13 (59)	8 (47)	0.74

Values are expressed as numbers and (%) or median and 25th - 75th, as appropriate. ANA, anti-nuclear antibodies; CK, creatine kinase; DLCO, diffusion lung CO; ENA, extractable nuclear antigen; FVC, forced vital capacity; ILD, interstitial lung disease; KCO, carbon monoxide transfer coefficient; MMT, manual muscle test; MRI, magnetic resonance imaging; MDA5, anti-melanoma differentiation-associated gene; NSIP, non-specific interstitial pneumonia; OP, organizing pneumonia; RNP, ribonucleoprotein; SAE, small ubiquitin-like modifier-1 activating enzyme; SRP, signal recognition particle; TIF1 γ , transcription intermediary factor 1-gamma; TLC, total lung capacity; UIP, usual interstitial pneumonia.

Table 3 Supplemental. Demographics, radiological and functional parameters at IIMs-ILD diagnosis of the IIM-ILD population, categorized among myositis phenotype.

	Total population n=78	PM n=17	DM n=20	ASyS n=41	p value
<i>Demographics</i>					
Male - <i>n (%)</i>	23 (29)	6 (35)	7 (35)	10 (24)	0.58
Female - <i>n (%)</i>	55 (71)	11 (65)	13 (65)	31 (76)	
Age at myositis diagnosis - <i>years</i>	57 (50-66)	62 (53-71)	57 (51-60)	57 (50-65)	0.25
Age at ILD diagnosis - <i>years</i>	57 (50-66)	62 (57-69)	57 (53-61)	57 (50-65)	0.22
Lag time symptoms-diagnosis - <i>years</i>	0 (0-1)	0.5 (0-1)	0 (0-1)	0 (0-1)	0.51
Time from myositis diagnosis to ILD - <i>years</i>	0 (0-0)	0 (-1-1)	0 (0-1)	0 (0-0)	0.14
Follow-up duration - <i>years</i>	4 (2-6)	6 (3-6)	4 (3-7)	4 (2-6)	0.55
Immunosuppressants - <i>n (%)</i>	41 (53)	9 (53)	14 (70)	18 (44)	0.16
Deaths - <i>n (%)</i>	1 (1)	1 (6)	0 (0)	0 (0)	0.22
<i>Radiographic pattern</i>					
NSIP - <i>n (%)</i>	17 (22)	9 (53)	13 (65)	17 (41)	0.33
UIP - <i>n (%)</i>	20 (26)	6 (35)	3 (15)	13 (32)	
OP - <i>n (%)</i>	41 (53)	2 (12)	4 (20)	11 (27)	
<i>Pulmonary function test</i>					
FVC - L	2.56 (2.16-3.21)	2.54 (2.11-3.19)	2.83 (2.57-3.2)	2.55 (2.16-3.21)	0.36
FVC - % pred.	84 (70-94)	86 (74-96)	87 (77-95)	83 (57-93)	0.26

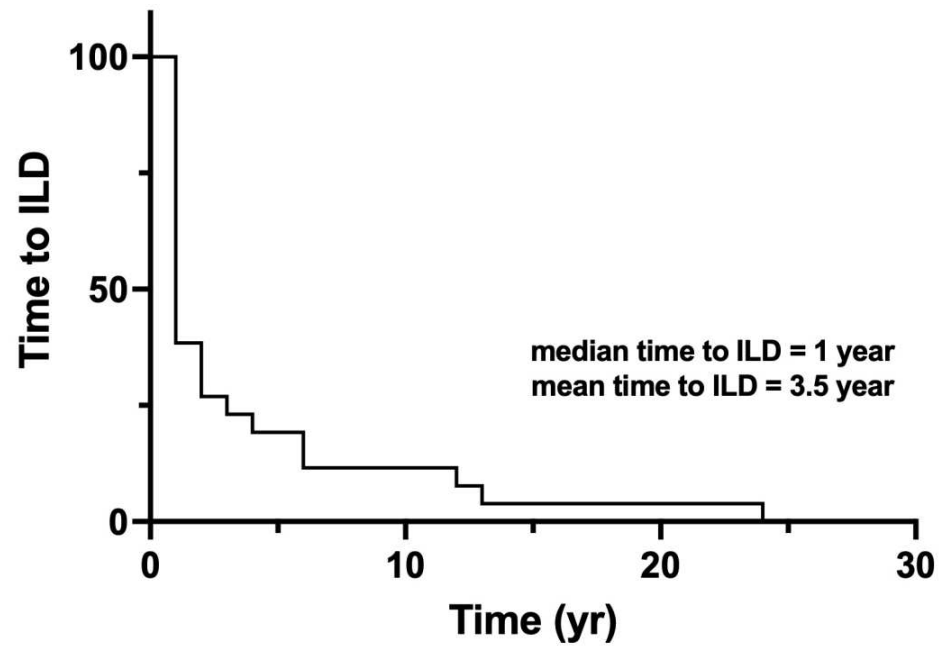
TLC - L	4.43 (3.56-4.97)	4.67 (4.06-5.11)	4.62 (3.70-5.53)	4.20 (3.25-4.64)	0.31
TLC - % pred.	81 (65-90)	82 (70-98)	81 (70-92)	79 (63-88)	0.41
DLCO - % pred.	58 (42-69)	68 (52-79)	50 (42-63)	56 (38-65)	0.08
KCO - % pred.	81 (64-90)	87 (84-94)	75 (68-85)	73 (55-88)	0.10

Values are expressed as numbers and (%) or median and Q1-Q3 as appropriate. CK, creatine kinase; DLCO, diffusion lung CO; KCO, carbon monoxide transfer coefficient; FVC, forced vital capacity; MMT, manual muscle test; NSIP, non-specific interstitial pneumonia; OP, organizing pneumonia; TLC, total lung capacity; UIP, usual interstitial pneumonia.

Table 4 Supplemental. Treatment of the IIM-ILD population during the first year after ILD diagnosis, categorized as progressors and non progressors.

	Total population n=78	PF-ILD n=14	Non PF-ILD n=64	p value
Systemic steroids – <i>n</i> (%)	69 (87)	13 (93)	56 (86)	0.49
• Initial dose - <i>mg</i>	25 (12.5 – 37.5)	25 (10 – 37.5)	25 (12.5 – 46.5)	0.61
Cyclophosphamide – <i>n</i> (%)	9 (11)	1 (7)	8 (12)	0.58
Methotrexate - <i>n</i> (%)	15 (19)	1 (7)	14 (21)	0.21
Mycophenolate Mofetil – <i>n</i> (%)	26 (33)	5 (36)	21 (32)	0.81
Azathioprine - <i>n</i> (%)	11 (14)	1 (7)	10 (15)	0.42
Cyclosporine – <i>n</i> (%)	5 (6)	0	5 (8)	0.28
Rituximab – <i>n</i> (%)	9 (11)	1 (7)	8 (12)	0.58
Intravenous immunoglobulin – <i>n</i> (%)	6 (8)	1 (7)	5 (8)	0.94

Values are expressed as numbers and (%) or median and ranges, as appropriate.



years	0	5	10	15	20	25
patients - n	26	5	3	1	0	0

Figure 1 Supplemental. Time (year) to ILD development after IIM diagnosis.

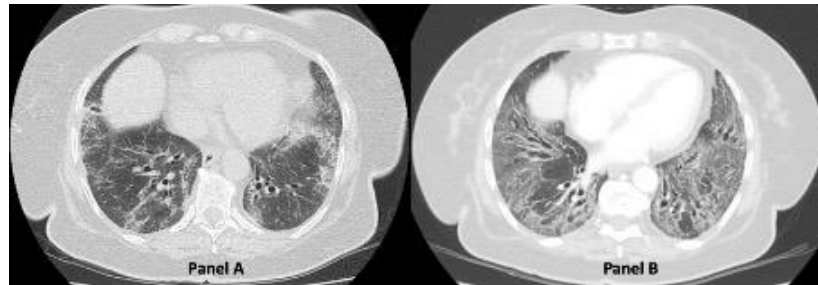


Figure 2 Supplemental. Radiographic progression after one year. CT images of a 77 year-old woman with antisynthetase syndrome (ASyS) positive for anti-PL12, anti-SSA and anti-Ro52 antibodies at baseline (Panel A) and after one year (Panel B) showing radiological features consistent with progression (17).