Myositis-specific Antibodies Identify a Distinct Interstitial Pneumonia with Autoimmune Features Phenotype

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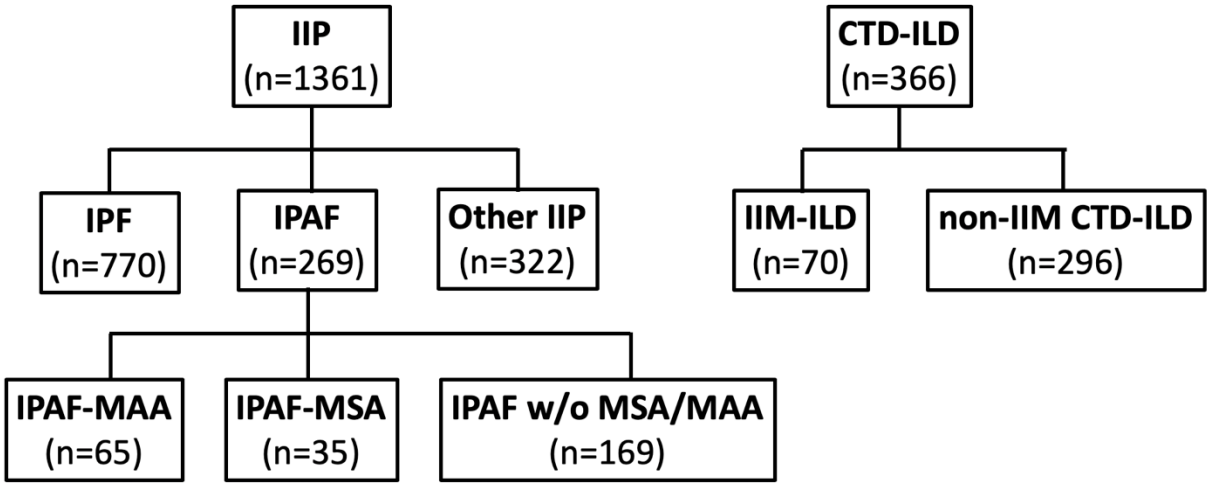

Figure S1. STROBE Diagram

Figure S2. Kaplan Meier Survival Curve for individual MAAs in IPAF-MAA cohort

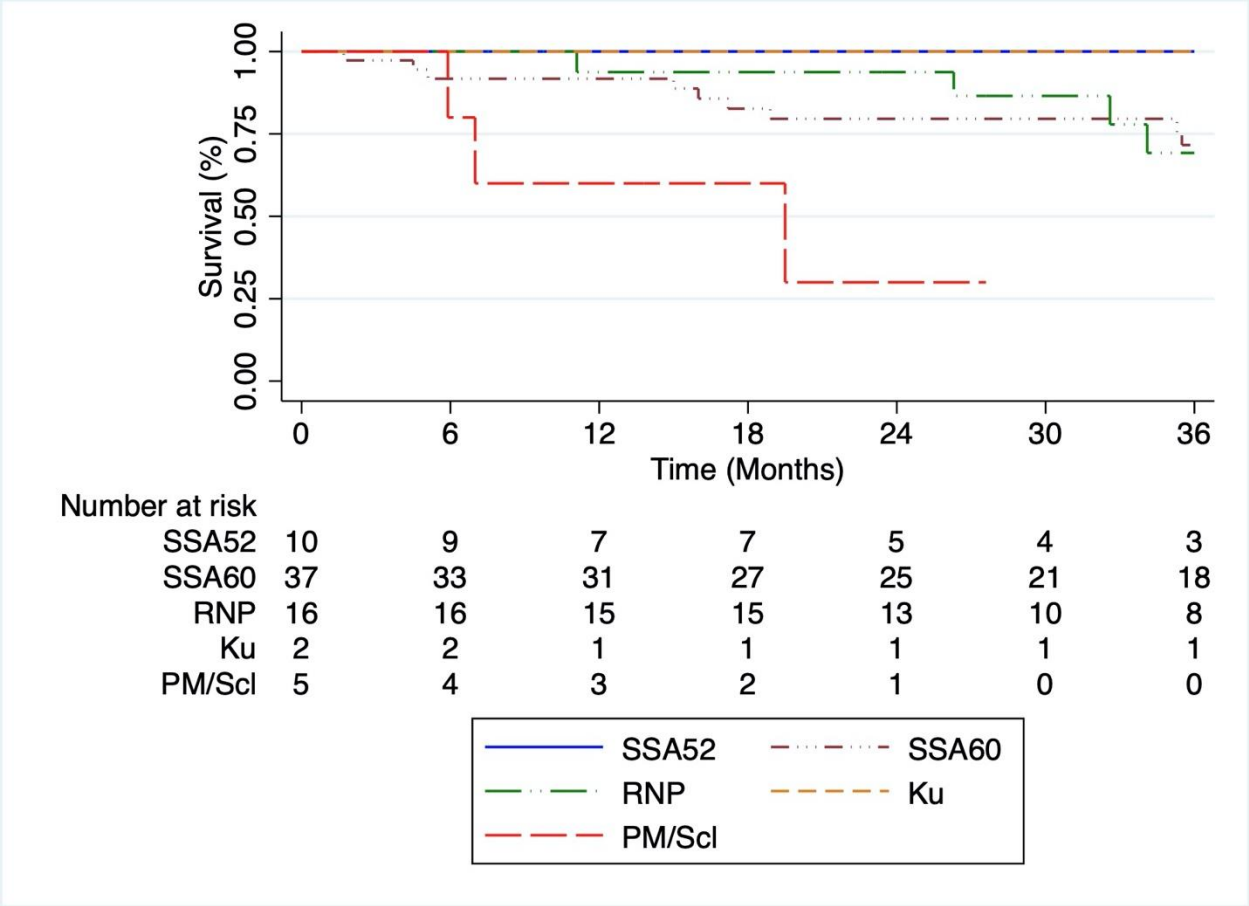

Table S1. Baseline characteristics among patients meeting IPAF criteria stratified by center

Demographics	**UC-Davis (n=62)**	**UChicago (n=146)**	**UTSW (n=73)**	**p-value**
Age, mean (SD)	66.6 (12.7)	61.9 (12.3)	60.5 (11.4)	0.01
Male, n (%)	21 (33.9)	64 (43.8)	33 (45.2)	0.33
Race/ethnicity, n (%)				
White	43 (69.4)	102 (69.9)	59 (80.8)	0.001
African American	3 (4.8)	30 (20.6)	6 (8.2)	
Hispanic	9 (14.5)	7 (4.8)	6 (8.2)	
Asian	5 (8.1)	7 (4.8)	2 (2.7)	
Mixed	2 (3.2)	0 (0)	0 (0)	
Ever smoker, n (%)	34 (54.8)	77 (52.7)	30 (41.1)	0.19
HRCT Pattern, n (%)				
Usual Interstitial Pneumonia	11 (17.7)	58 (45.7)	22 (30.1)	<0.001
Non-specific Interstitial Pneumonia	20 (32.3)	65 (45.5)	33 (45.2)	
Non-specific Interstitial Pneumonia with Organizing PNA	2 (3.2)	16 (11.2)	6 (8.2)	
Organizing Pneumonia	5 (8.1)	4 (2.8)	1 (1.4)	
Other	24 (38.7)	8 (5.6)	11 (15.1)	
SLB Pattern				
Usual Interstitial Pneumonia	9 (36.0)	57 (70.4)	15 (39.5)	0.001
Non-specific Interstitial Pneumonia	7 (28.0)	10 (12.4)	17 (44.7)	
Organizing Pneumonia	5 (20.0)	8 (9.9)	3 (7.9)	
Other	4 (16.0)	6 (7.4)	3 (7.9)	
Pulmonary Function				
Forced vital capacity (% predicted), mean (SD)	68.9 (19.2)	60.9 (18.5)	66.3 (23.2)	0.02
Diffusion capacity (% predicted), mean (SD)	50.1 (18.2)	44.8 (18.9)	44.9 (18.9)	0.17
IPAF Domains				
Clinical domain met, n (%)	38 (61.3)	81 (55.5)	27 (37)	0.01
Serologic domain met, n (%)	57 (91.9)	136 (91.2)	71 (97.3)	0.37
Morphologic domain met, n (%)	43 (69.4)	116 (79.5)	67 (91.8)	0.004
IPAF Criteria				
IPAF due to clinical and serologic criteria, n (%)	19 (30.7)	30 (20.6)	6 (8.2)	0.01
IPAF due to clinical and morphologic criteria, n (%)	5 (8.0)	10 (6.9)	2 (2.7)	
IPAF due to serologic and morphologic criteria, n (%)	24 (38.7)	65 (44.5)	46 (63)	
IPAF due to clinical, serologic and morphologic criteria, n (%)	14 (22.6)	41 (28.1)	19 (26)	
Treatment and Outcomes				
Any immunosuppressant, n (%)	37 (59.7)	55 (37.7)	41 (56.2)	0.003
Death, n (%)	12 (19.4)	43 (29.5)	13 (17.8)	0.11
Transplant, n (%)	0 (0)	7 (8.1)	4 (15.4)	0.15
Death or Transplant, n (%)	12 (19.4)	50 (34.3)	17 (23.3)	0.06
Follow-up time, median (IQR)	23.8 (15.2-28.0)	26.3 (8.2-36.0)	36 (28.9-36.0)	<0.001

Table S2. Unadjusted outcome risk for ILD subgroups stratified by center

ILD Subtype	UC-Davis			UChicago			UTSW		
	n	HR	95% CI	n	HR	95% CI	n	HR	95% CI
IPAF without MSA/MAA	25	Ref	Ref	98	Ref	Ref	46	Ref	Ref
IPAF-MSA	19	0.14	0.02-1.15	6	*	*	10	0.35	0.04-2.68
IPAF-MAA	18	0.52	0.14-1.96	30	0.50	0.23-1.06	17	1.41	0.49-4.06
IIM-ILD	17	0.16	0.02-1.26	35	0.10	0.02-0.40	18	*	*
Other CTD-ILD	55	0.46	0.18-1.20	154	0.33	0.20-0.54	87	0.48	0.21-1.11
IPF	114	0.83	0.38-1.80	352	1.09	0.77-1.54	304	1.73	0.93-3.22

Abbreviations: ILD = interstitial lung disease; IPAF = interstitial pneumonia with autoimmune features; MSA = myositis specific antibody; IIM-ILD = idiopathic inflammatory myopathy-associated ILD; IPF = idiopathic pulmonary fibrosis

* Unable to estimate given no events

Table S3. Outcome risk for ILD subgroups with covariate point estimates reported

ILD Subtype	Unadjusted			Adjusted		
	HR	95% CI	p-value	HR	95% CI	p-value
Model 1*						
IPAF without MSA/MAA	Ref	Ref	Ref	Ref	Ref	Ref
IPAF-MSA	0.13	0.03-0.55	0.005	0.20	0.05-0.84	0.03
IPAF-MAA	0.65	0.37-1.12	0.12	0.68	0.38-1.21	0.19
IIM-ILD	0.09	0.03-0.30	<0.001	0.17	0.05-0.54	0.003
non-IIM CTD-ILD	0.37	0.25-0.55	<0.001	0.52	0.34-0.80	0.003
IPF	1.11	0.84-1.46	0.47	0.70	0.51-0.97	0.03
Center (UCD reference)						
Chicago	1.53	1.14-2.06	0.01	1.44	1.06-1.95	0.02
UTSW	1.04	0.76-1.42	0.83	1.24	0.89-1.71	0.21
White race/ethnicity	1.58	1.24-2.02	<0.001	1.01	0.77-1.32	0.95
UIP present	3.02	2.26-4.04	<0.001	1.43	0.97-2.10	0.07
IS exposure	0.35	0.27-0.45	<0.001	0.64	0.47-0.87	0.005
GAP Stage (one-unit increase)	2.65	2.31-3.04	<0.001	2.41	2.08-2.78	<0.001
Model 2∫						
IPAF-UIP	Ref	Ref	Ref	Ref	Ref	Ref
IPAF w/o UIP	0.37	0.23-0.61	<0.001	0.46	0.28-0.78	0.004
IPAF-MSA	0.10	0.02-0.41	0.001	0.14	0.03-0.58	0.007
IIM-ILD	0.07	0.02-0.23	<0.001	0.13	0.04-0.42	0.001
non-IIM CTD-ILD	0.28	0.19-0.42	<0.001	0.43	0.27-0.66	<0.001
IPF	0.83	0.62-1.11	0.22	0.63	0.46-0.86	0.003
Center (UCD reference)						
Chicago	1.53	1.14-2.06	0.01	1.44	1.06-1.94	0.02
UTSW	1.04	0.76-1.42	0.83	1.24	0.90-1.72	0.19
White race/ethnicity	1.58	1.24-2.02	<0.001	1.03	0.79-1.34	0.83
IS exposure	0.35	0.27-0.45	<0.001	0.64	0.47-0.86	0.004
GAP Stage (one-unit increase)	2.65	2.31-3.04	<0.001	2.40	2.08-2.77	<0.001

* Model 1 adjusted for center, race/ethnicity, presence of UIP, immunosuppressant exposure and GAP stage

∫ Model 2 adjusted for center, race/ethnicity, immunosuppressant exposure and GAP stage

Abbreviations: ILD = interstitial lung disease; IPAF = interstitial pneumonia with autoimmune features; MSA = myositis specific antibody; IIM-ILD = idiopathic inflammatory myopathy-associated ILD; IPF = idiopathic pulmonary fibrosis