Online Data Supplement to "Imaging Patterns are Associated with Interstitial Lung Abnormality Progression and Mortality"

RESULTS

Table E1. Baseline characteristics of participants stratified by interstitial lung abnormality (ILA) status on the second CT scan*

	No ILA† (0) (N=1792, 57%)	Indeterminate (1) (N=1091, 34%)	ILA (2) (N=284, 9%)	P-Value	
				All	0 vs 2
Age, years	74 ± 5	76 ± 5	76 ± 5	<0.0001	<0.0001
Sex - female - male	1082 (60%) 710 (40%)	621 (57%) 470 (43%)	128 (45%) 156 (55%)	<0.0001	<0.0001
Body Mass Index (kg/m^2)	27 ± 4	27 ± 2	28 ± 4	0.8	0.02
Pack-Years Smoking, median (IQR‡)	0 (15)	2 (20)	11 (31)	<0.0001	<0.0001
Smoking Status - Never - Former - Current	848 (47%) 756 (42%) 188 (11%)	449 (41%) 522 (48%) 120 (11%)	78 (27%) 169 (60%) 36 (13%)	<0.0001	<0.0001
MUC5B‖ - *GG* - *GT* - *TT*	1436 (80%) 340 (19%) 15 (1%)	800 (73%) 274 (25%) 15 (1%)	168 (59%) 105 (37%) 10 (4%)	<0.0001	<0.0001

* ± values are means ± standard deviation
† ILA is interstitial lung abnormality
‡ IQR is interquartile range
‖ *MUC5B* is the genotype at the *MUC5B* promoter polymorphism (rs35705950). The total N for genotype may be less than the N for each ILA subtype, as it is based on the number of participants with genotype available, and due to rounding not all percentages add to 100%.

Table E2. Multivariable logistic regression to assess factors associated with ILA progression, comparing those with imaging progression to those without imaging progression and comparing those with imaging progression to those without ILA on either CT scan, where ILA is limited to those with an indeterminate for UIP pattern.

Covariate	Comparison of ILA with Progression to ILA without Progression	P-Value	Comparison of ILA with Progression to No ILA	P-Value
	OR* (95% CI†)		OR (95% CI)	
MUC5B Genotype‡	2.5 (1.2, 4.9)	0.01	2.6 (1.9, 3.5)	<0.0001
Age‖	1.05 (0.98, 1.1)	0.2	1.08 (1.04, 1.1)	<0.0001
Sex¶	0.8 (0.4, 1.6)	0.6	0.6 (0.4, 0.8)	0.0006
Body-Mass Index§	1.04 (0.96, 1.1)	0.4	1.08 (1.04, 1.1)	0.0001
Pack-years smoking**	1.0 (0.98, 1.01)	0.6	1.01 (1.005, 1.02)	0.0006
Current Smoking Status††	1.2 (0.4, 3.7)	0.7	0.9 (0.5, 1.6)	0.7

*OR is odds ratio
†CI is confidence interval
‡OR is per copy of *MUC5B* minor allele
‖OR is for each additional year older.
¶OR is for comparison of female to male.
§OR is for 1 kg/m^2 increase in body-mass index.
**OR is for each additional pack-year smoked.
††OR is for the comparison of current to former/never.

Table E3. Multivariable logistic regression to assess factors associated with ILA progression, comparing those with imaging progression to those without imaging progression.

Covariate	Comparison of ILA with Progression to ILA without Progression	P-Value
	OR* (95% CI†)	
MUC5B Genotype‡	3.4 (1.7, 6.9)	0.0006
Age‖	1.06 (0.99, 1.14)	0.1
Sex¶	0.6 (0.3, 1.2)	0.2
Body-Mass Index§	0.97 (0.9, 1.05)	0.5
Pack-years smoking**	1.005 (0.99, 1.02)	0.5
Current Smoking Status††	1.4 (0.5, 4.1)	0.6
Centrilobular Nodules	0.2 (0.1, 0.5)	0.0002

*OR is odds ratio
†CI is confidence interval
‡OR is per copy of *MUC5B* minor allele
‖OR is for each additional year older.
¶OR is for comparison of female to male.
§OR is for 1 kg/m^2 increase in body-mass index.
**OR is for each additional pack-year smoked.
††OR is for the comparison of current to former/never.

Table E4. Multivariable logistic regression to assess factors associated with ILA progression, comparing those with imaging progression to those without imaging progression.

Covariate	Comparison of ILA with Progression to ILA without Progression	P-Value
	OR* (95% CI†)	
MUC5B Genotype‡	3.4 (1.7, 6.9)	0.0007
Age‖	1.08 (1.02, 1.1)	0.06
Sex¶	0.6 (0.3, 1.3)	0.2
Body-Mass Index§	1.0 (0.9, 1.1)	0.9
Pack-years smoking**	1.01 (0.98, 1.02)	0.5
Current Smoking Status††	1.5 (0.5, 4.7)	0.5
Subpleural Reticular Markings	6.4 (2.2, 19)	0.0008

*OR is odds ratio
†CI is confidence interval
‡OR is per copy of *MUC5B* minor allele
‖OR is for each additional year older.
¶OR is for comparison of female to male.
§OR is for 1 kg/m^2 increase in body-mass index.
**OR is for each additional pack-year smoked.
††OR is for the comparison of current to former/never.

Table E5. Multivariable logistic regression to assess factors associated with ILA progression, comparing those with imaging progression to those without imaging progression.

Covariate	Comparison of ILA with Progression to ILA without Progression	P-Value
	OR* (95% CI†)	
MUC5B Genotype‡	3.6 (1.8, 7.1)	0.0003
Age‖	1.08 (0.99, 1.2)	0.08
Sex¶	0.5 (0.3, 1.1)	0.09
Body-Mass Index§	1.01 (0.94, 1.1)	0.7
Pack-years smoking**	1.002 (0.98, 1.02)	0.8
Current Smoking Status††	1.0 (0.3, 3.0)	1.0
Nonemphysematous Cysts	2.5 (1.8, 7.1)	0.009

*OR is odds ratio
†CI is confidence interval
‡OR is per copy of *MUC5B* minor allele
‖OR is for each additional year older.
¶OR is for comparison of female to male.
§OR is for 1 kg/m^2 increase in body-mass index.
**OR is for each additional pack-year smoked.
††OR is for the comparison of current to former/never.

Table E6. Multivariable logistic regression to assess factors associated with ILA progression, comparing those with imaging progression to those without imaging progression.

Covariate	Comparison of ILA with Progression to ILA without Progression OR* (95% CI†)	P-Value
MUC5B Genotype‡	5.0 (1.8, 13)	0.002
Age‖	1.08 ().97, 1.2)	0.2
Sex¶	0.4 (0.2, 1.1)	0.08
Body-Mass Index§	1.0 (0.9, 1.1)	1.0
Pack-years smoking**	1.05 (1.006, 1.09)	0.02
Current Smoking Status††	1.4 (0.2, 8.4)	0.7
Lower Lobe Predominant Changes	6.7 (1.8, 25)	0.004

*OR is odds ratio
†CI is confidence interval
‡OR is per copy of *MUC5B* minor allele
‖OR is for each additional year older.
¶OR is for comparison of female to male.
§OR is for 1 kg/m^2 increase in body-mass index.
**OR is for each additional pack-year smoked.
††OR is for the comparison of current to former/never.

Table E7. Multivariable logistic regression to assess factors associated with ILA progression, comparing those with imaging progression to those without imaging progression.

Covariate	Comparison of ILA with Progression to ILA without Progression	P-Value
	OR* (95% CI†)	
MUC5B Genotype‡	3.7 (1.8, 7.7)	0.0004
Age‖	1.07 (0.99, 1.2)	0.09
Sex¶	0.5 (0.2, 1.1)	0.07
Body-Mass Index§	1.03 (0.95, 1.1)	0.5
Pack-years smoking**	1.0 (0.99, 1.02)	0.9
Current Smoking Status††	0.99 (0.3, 3.1)	1.0
Traction Bronchiectasis	6.6 (2.3, 19)	0.0004

*OR is odds ratio
†CI is confidence interval
‡OR is per copy of *MUC5B* minor allele
‖OR is for each additional year older.
¶OR is for comparison of female to male.
§OR is for 1 kg/m^2 increase in body-mass index.
**OR is for each additional pack-year smoked.
††OR is for the comparison of current to former/never.

Table E8. Radiologic features and imaging patterns on CT scan with ILA, at baseline (Round 1) and follow up (Round 2), with round 1 subset by ILA cases with a follow up scan*

	Round 1 (All ILA Cases, N=378)	Round 1 (ILA cases with follow up scan, N=172)	Round 2 (All ILA cases, N=284)
Ground Glass	378 (100%)	172 (100%)	284 (100%)
Centrilobular Nodules	126 (33%)	66 (38%)	70 (25%)
Reticular Markings	337 (89%)	146 (85)	258 (91%)
Nonemphysematous Cysts	225 (60%)	97 (56%)	174 (61%)
Traction Bronchiectasis	138 (34%)	47 (27%)	67 (24%)
Honeycombing	16 (4%)	5 (3%)	8 (3%)
Lower Lobe Predominant	250 (66%)	103 (60%)	207 (73%)
Upper Lobe Predominant	29 (8%)	18 (10%)	16 (6%)
Diffuse	71 (19%)	38 (22%)	37 (13%)
Multifocal	28 (7%)	13 (8%)	23 (8%)
Subpleural Subtype	237 (63%)	102 (59%)	188 (66%)
Centrilobular Subtype	39 (10%)	26 (15%)	22 (8%)
Mixed Subtype	85 (22%)	39 (23%)	51 (18%)
Radiologic Evidence of ILD‡	17 (5%)	5 (3%)	23 (8%)
Definite Fibrosis	129 (34%)	46 (27%)	70 (25%)
Without Fibrosis	249 (66%)	126 (73%)	214 (75%)
Non-IPF‡ Diagnosis	145 (38%)	70 (41%)	84 (30%)
Indeterminate for UIPǁ	134 (35%)	67 (39%)	139 (49%)
Probable UIP	82 (22%)	30 (17%)	54 (19%)
UIP	17 (5%)	5 (3%)	7 (2%)

*ILA is interstitial lung abnormality
†ILD is interstitial lung disease
‡IPF is idiopathic pulmonary fibrosis
ǁUIP is usual interstitial pneumonia

Table E9. Association between imaging patterns and interstitial lung abnormality (ILA) progression.

	Unadjusted Analysis OR† (95% CI‡)	P-Value	Adjusted* Analysis OR (95% CI)	P-Value
Definite Fibrosis	7.2 (2.7-20)	<0.0001	8.4 (2.7-26)	0.0003
Subpleural Predmoninantǁ	9.7 (3.5-27)	<0.0001	9.1 (2.7-30)	0.0003
Mixed¶	3.9 (1.3-12)	0.02	3.3 (0.99-11)	0·05
Radiologic Evidence of ILD§	--	--	--	--

*Adjusted for age, sex, *MUC5B* minor allele, and smoking behavior.

†OR=odds ratio

‡CI=confidence interval

ǁComparison is made to centrilobular predominant ILA

¶Mixed=combination of subpleural and centrilobular, comparison is made to centrilobular predominant ILA

§ILD=interstitial lung disease, no comparisons could be made as all participants with radiologic evidence of ILD had imaging progression.

Table E10. Imaging pattern and progression information of the five participants with definite fibrosis on the first CT* scan that did not have imaging progression.

	Imaging Pattern Baseline CT Scan	Progression	Imaging Pattern Follow-up CT Scan
Participant 1	Mixed subpleural and centrilobular / consistent with non-IPF† diagnosis	No change	Predominantly Subpleural / Indeterminate for UIP‡
Participant 2	Mixed subpleural and centrilobular / consistent with non-IPF diagnosis	No change	Mixed subpleural and centrilobular / consistent with non-IPF diagnosis
Participant 3	Mixed subpleural and centrilobular / consistent with non-IPF diagnosis	No Change	Indeterminate for ILA‖
Participant 4	Mixed subpleural and centrilobular / consistent with non-IPF diagnosis	Probably improved	Indeterminate for ILA
Participant 5	Mixed subpleural and centrilobular / consistent with non-IPF diagnosis	Probably improved	Mixed subpleural and centrilobular / consistent with non-IPF diagnosis

*CT is computed tomography
†IPF is idiopathic pulmonary fibrosis
‡UIP=usual interstitial pneumonia
‖ ILA=interstitial lung abnormalities

Table E11. Association between imaging pattern and mortality.

	Unadjusted Analysis	P-value	Adjusted* Analysis	P-value
	HR† (95% CI‡)		HR (95% CI)	
Alternate Non-IPF¶ Diagnosis without fibrosis‖	1.4 (1.3-2.0)	0.0001	1.5 (1.2-2.0)	0.0003
Alternate Non-IPF Diagnosis with fibrosis‖	3.0 (2.0-4.4)	<0.0001	2.0 (1.4-3.0)	0.0006

* Adjusted analyses are adjusted for age, sex, pack-years smoking, current smoking status, and body-mass index.
†HR is hazard ratio
‡CI=confidence interval
¶IPF=idiopathic pulmonary fibrosis.
‖Comparisons are to participants without interstitial lung abnormalities.