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3 **On-line supplemental data**  
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7 **Table S1. Demographic features and age of diagnosis of 94 TSC-LAM patients**  
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10	<b>Number of patients</b>	94
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12	<b>TSC diagnosed before LAM</b>	61 (64.8 %)
13		
14	Age of LAM diagnosis	36±10.4 (18-63)
15		
16	Age of TSC diagnosis	18.3±14.7 (0-52)
17		
18	Admitted as TSC (screening protocol)	38 (40.4 %)
19		
20	Diagnosed with TSC at NIH	22 (23.4 %)
21		
22	<b>LAM diagnosed before TSC</b>	26 (27.7 %)
23		
24	Age of LAM diagnosis	37±10.4 (23-60)
25		
26	Age of TSC diagnosis	41.6±10.6 (23-63)
27		
28	Admitted as LAM (LAM protocol)	56 (59.6 %)
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30	<b>TSC and LAM diagnosed at same time</b>	7 (7.4 %)
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32	Age of TSC/LAM diagnosis	37.4±12 (17-57)
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**Table S2. Pulmonary function data in patients with TSC-LAM and sporadic LAM at time of the first visit**

	TSC-LAM	Sporadic LAM
Number of patients	94	460
TLC (liters)	4.9±0.9	4.9±0.9
% TLC	94.9±12.8	94.5±16.3
FRC (liters)	2.6±0.6	2.7±0.7
% FRC	94.0±18.2	96.7±24.2
RV (liters)	1.7±0.5	1.8±0.6
% RV	103.5±29.3*	107.3±37.8
% RV/TLC	34.9±8.6*	36.7±9.4
FVC (liters)	3.2±0.8	3.0±0.7
% FVC	90.0±20.3	88.1±18.5
FEV <sub>1</sub> (liters)	2.3±0.8	2.0±0.7
% FEV <sub>1</sub>	82.7±27.5*	75.2±24.9
% FEV <sub>1</sub> /FVC	70.3±16.3	65.7±16.1
DL <sub>CO</sub> (ml/min/mmHg)	18.2±8.0	15.2±5.7
% DL <sub>CO</sub>	80.3±29.1*	70.7±25.8

\* p<0.05. Data are shown as mean±SD. Abbreviations used are: TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; RV/TLC, ratio between RV and TLC; FEV<sub>1</sub>, forced expiratory volume in the first second; FVC, forced vital capacity; FEV<sub>1</sub> /FVC, ratio of FEV<sub>1</sub> to FVC; DL<sub>CO</sub>, diffusion capacity for carbon monoxide.

**Table S3. Initial pulmonary function and clinical data in 73 patients with TSC-LAM and 319 patients with sporadic LAM followed for approximately five years**

	TSC-LAM	Sporadic LAM
Number of patients	73	319
Age first visit	40.3±10.4	44.2±8.9
Age of diagnosis	38.0±10.7	41.5±9.2
Age first symptoms	34.2±10.3	38.0±9.5
Years of follow-up	5.3±3.0	4.9±3.0
Body mass index	26.6±5.9	26.1±5.9
TLC (liters)	4.9±0.8	4.9±0.9
% TLC	94.4±14.7	95.3±15.4
FRC (liters)	2.6±0.6	2.7±0.7
% FRC	94.1±21.5	97.6±22.7
RV (liters)	1.7±0.5	1.8±0.5
% RV	101.7±31.3*	106.1±31.4
% RV/TLC	34.7±8.8*	36.5±8.1
FVC (liters)	3.3±0.7	3.1±0.7
% FVC	91.8±18.0	89.0±18.0
FEV <sub>1</sub> (liters)	2.3±0.7	2.0±0.7
% FEV <sub>1</sub>	84.9±26.5*	76.1±24.9
% FEV <sub>1</sub> /FVC	71.2±16.2*	65.1±15.8
DL <sub>CO</sub> (ml/min/mmHg)	18.3±5.8	15.1±5.5
% DL <sub>CO</sub>	84.5±26.0*	71.6±24.4

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5 \*  $p < 0.05$ . Data are shown as mean  $\pm$  SD. For abbreviations, see on-line supplemental  
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7 data Table 1.  
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**Table S4- Exercise physiology at the time of initial testing in 76 patients with TSC-LAM and 340 patients with sporadic LAM**

	TSC-LAM	Sporadic LAM
Number of patients	76	340
Work rate (%)	86.8±32.7	90.7±30.5
HR max (beats/min)	153.0±21.4	151.4±19.5
HR max (%)	86.0±10.5	86.7±10.4
VO <sub>2</sub> max (ml/min)	1275±435	1259±438
VO <sub>2</sub> max (%)	72.1±21.5	74.6±23.4
VO <sub>2</sub> /HR max (ml/beat)	8.2±2.4	8.2±2.4
VO <sub>2</sub> /HR max (%)	83.0±21.2	86.1±24.2
VE max (l/min)	52.5±17.9 †	54.0±16.9
VE max (%)	57.2±16.1 *	67.6±18.7
BR (%)	42.5±16.5 *	31.3±18.3
VE/VCO <sub>2</sub> max	35.3±7.5	37.9±8.4
VE/VCO <sub>2</sub> at AT	33.4±7 †	36.9±7.4
RER at AT	1.01±0.06	1.0±0.05
RER max	1.19±0.15	1.17±0.15
SaO <sub>2</sub> at rest (%)	97.8±2.1	97.5±2.1
SaO <sub>2</sub> at peak exercise (%)	95.7±4.3	95.0±4.1
Decline in SaO <sub>2</sub> (%)	2.1±3.2	2.5±3.1

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4 Data are shown as means  $\pm$ SD. Abbreviations: HR max: peak heart rate; VO<sub>2</sub> max:  
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6 peak oxygen consumption; VE max: minute ventilation at peak exercise; BR: breathing  
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8 reserve; VE/VCO<sub>2</sub>: ventilatory equivalent for carbon dioxide; AT: anaerobic threshold;  
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10 RER: respiratory equivalent ratio; SaO<sub>2</sub>: pulse oxygen saturation (%). \* p < 0.05, † p <  
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12 0.01, using paired t test.  
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**Table S5. Changes in cyst scores in 40 patients with TSC-LAM and 40 patients with sporadic LAM followed for approximately six and one half years**

Pair number	TSC-LAM		Sporadic LAM	
	Initial cyst score (%)	Final cyst score (%)	Initial cyst score (%)	Final cyst score (%)
1	6.3	13.3	3.5	18.5
2	3.8	28.0	1.9	21.8
3	2.8	5.5	3.9	11.5
4	5.4	15.2	4.7	33.4
5	9.1	13.5	6.2	33.7
6	2.8	2.8	3.0	18.3
7	3.7	10.3	4.1	12.2
8	3.3	19.4	0.57	5.7
9	3.62	4.7	1.5	10.6
10	1.5	4.9	4.8	17.5
11	3.8	37.2	9.5	37.0
12	16.7	20.6	1.5	3.7
13	1.0	4.1	3.1	13.4
14	0.2	1.9	4.9	24.4
15	1.5	4.6	0.9	5.5
16	0.1	1.9	1.0	1.4

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2					
3	17	1.3	5.4	8.4	16.2
4					
5	18	0.6	4.7	0.7	5.5
6					
7					
8	19	0.8	4.0	5.2	10.3
9					
10					
11	20	2.6	6.6	12.3	13.9
12					
13	21	14.2	12.1	11.1	23.2
14					
15					
16	22	2.0	1.3	9.3	9.2
17					
18					
19	23	1.6	4.2	3.3	9.0
20					
21	24	1.4	4.0	1.2	4.0
22					
23					
24	25	0.5	2.4	4.1	16.3
25					
26	26	1.1	1.0	3.2	4.7
27					
28					
29	27	11.1	19.4	5.1	13.0
30					
31					
32	28	6.4	11.9	3.8	7.6
33					
34					
35	29	17.3	28.8	2	5.5
36					
37	30	8.3	13.9	3.2	7.6
38					
39					
40	31	26.6	29.4	6.3	11.5
41					
42					
43	32	3.2	16.4	30	41.2
44					
45					
46	33	7.2	25.3	6	31.7
47					
48	34	6	19.7	6.9	28.9
49					
50					
51	35	9.9	23	9.5	16.6
52					
53					
54	36	1.2	5.1	7.4	13.6
55					
56	37	0.6	2.2	5.3	10.2
57					
58					
59					
60					



1					
2					
3	38	1.8	5.5	2	10.3
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5	39	18.5	26.6	14.7	17.5
6					
7					
8	40	4.6	11.8	12.2	17.2
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**Figure legend**

Figure S1. Changes in percentage of lung volume occupied by cysts (cyst scores) in 40 patients with TSC-LAM and 40 age- and lung function-matched sporadic LAM patients over a period of approximately six and one half years. Panel A: TSC-LAM: Fourteen patients had an yearly increase in cyst scores of one percent or greater; in six patients, cyst scores remained unchanged. Panel B: Sporadic LAM: Twenty-six patients had an yearly increase in cyst scores equal to or greater than one percent. Only three patients had no change in cyst scores.

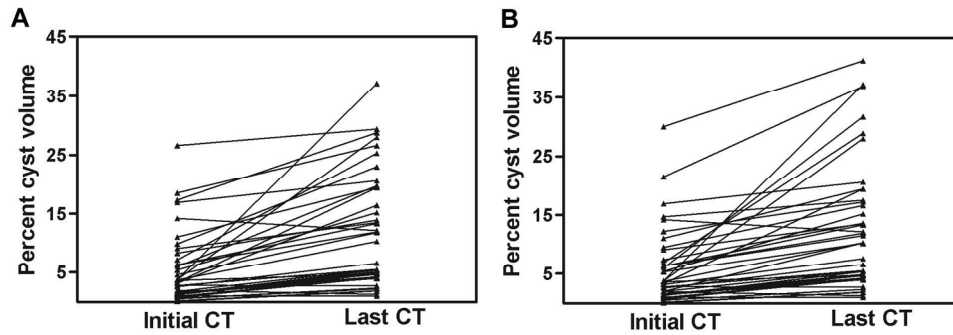


Figure S1. Changes in percentage of lung volume occupied by cysts (cyst scores) in 40 patients with TSC-LAM and 40 age- and lung function-matched sporadic LAM patients over a period of approximately six and one half years. Panel A: TSC-LAM: Fourteen patients had an yearly increase in cyst scores of one percent or greater; in six patients, cyst scores remained unchanged. Panel B: Sporadic LAM: Twenty-six patients had an yearly increase in cyst scores equal to or greater than one percent. Only three patients had no change in cyst scores.

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