

Supplementary Tables:

Table S1. Distribution of Facial Angiofibromas in Patients with Mosaic Tuberous Sclerosis Complex.

P#	Mosaic Subtype	Total^a	L	R	Predominance
20	Asym	10	0	10	100%
40	Asym	43	40	3	93%
49	Asym	49	4	45	92%
31	Asym	10	1	9	90%
33	Asym	32	6	26	81%
29	Asym	33	8	25	76%
25	Asym	91	68	23	75%
3	Sym	126	58	68	54%
39	Sym	19	9	10	53%
19	Sym	92	49	43	53%
21	Sym	368	173	195	53%
10	Sym	17	8	9	53%
14	Sym	50	24	26	52%
11	Sym	271	131	140	52%
12	Sym	72	37	35	51%
5	Sym	386	189	197	51%
30	Sym	14	7	7	50%
32	Sym	6	3	3	50%
4	Sym	600+	300+	300+	50%

^aTotal number of angiofibromas on the nose and cheeks.

Abbreviations: L, Left; R, Right; Asym, Asymmetrical; Sym, Symmetrical.

Table S2. The Median Number of Mucocutaneous, Internal, and Total Findings Differs Between Patients with Germline Disease, Symmetrical-Angiofibroma Mosaicism, and Asymmetrical-Angiofibroma Mosaicism.

	Germline (G)	Sym-AF Mosaic (Sym)	Asym-AF Mosaic (Asym)	P-Values		
				G vs. Sym	G vs. Asym	Sym vs. Asym
MCF (8 Max)	6 (1 – 8) n=28	4 (2 – 6) n=12	1 (1 – 4) n=7	0.001	<0.001	0.002
IF (5 Max)	4 (2 – 5) n=26	4 (0 – 5) n=12	3 (1 – 3) n=7	0.920	0.003	0.012
Total (13 Max)	10 (8 – 12) n=25	8 (3 – 11) n=12	4 (3 – 7) n=7	0.004	<0.001	0.004

Abbreviations: MCF, Mucocutaneous Findings; IF, Internal Findings; Sym-AF, Symmetrical-Angiofibroma; Asym-AF, Asymmetrical-Angiofibroma.

Data displayed as median (range). Bold text indicates significant p-values <0.05. P-values were determined using Mann-Whitney test. A finding was defined as present if sufficient to meet diagnostic criteria (AF \geq 3, HM \geq 3, UF \geq 2, DP \geq 3, and OF \geq 2).

Table S3. Characteristics of Patients with Asymmetrical-Angiofibroma Mosaicism, Symmetrical-Angiofibroma Mosaicism, or Germline Tuberous Sclerosis Complex.

	Germline (G)	Sym-AF Mosaic (Sym)	Asym-AF Mosaic (Asym)	P-Values		
				G vs. Sym	G vs. Asym	Sym vs. Asym
MUCOCUTANEOUS						
HM	28/29 (97%)	10/12 (83%)	2/7 (29%)	0.200	<0.001	0.045
FCP	19/29 (66%)	4/12 (33%)	1/7 (14%)	0.087	0.030	0.600
SP	15/29 (52%)	8/12 (67%)	0/7 (0%)	0.497	0.027	0.013
UF	29/29 (100%)	9/12 (75%)	1/7 (14%)	0.021	<0.001	0.012
AF	27/29 (93%)	12/12 (100%)	7/7 (100%)	1	1	1
Confetti	10/29 (34%)	3/12 (25%)	1/7 (14%)	0.719	0.400	1
DP	27/29 (93%)	7/12 (58%)	4/7 (57%)	0.016	0.040	1
OF	24/28 (86%)	4/12 (33%)	3/7 (43%)	0.002	0.034	1
NEUROLOGICAL						
Tuber	28/28 (100%)	10/12 (83%)	6/7 (86%)	0.084	0.200	1
SEN	20/26 (77%)	8/12 (67%)	0/7 (0%)	0.694	<0.001	0.013
SEGA	5/26 (19%)	3/12 (25%)	0/7 (0%)	1	0.559	0.263
RH	10/17 (59%)	3/10 (30%)	1/7 (14%)	0.237	0.078	0.603
Seizure	14/29 (48%)	3/12 (25%)	1/7 (17%)	0.296	0.200	1
PULMONARY & RENAL						
LAM	23/29 (79%)	11/12 (92%)	5/7 (71%)	0.651	0.639	0.523
Pneumothorax ^a	11/23 (48%)	6/11 (55%)	2/5 (40%)	1	1	1
AML	25/29 (86%)	11/12 (92%)	6/7 (85%)	1	1	1
PKD	2/29 (7%)	0/12 (0%)	0/7 (0%)	1	1	1
Nephrectomy ^b	9/26 (34%)	3/11 (27%)	2/6 (33%)	1	1	1
Renal Transplant ^b	2/26 (8%)	0/11 (0%)	0/6 (0%)	1	1	1
Embolization ^b	3/26 (12%)	3/11 (27%)	4/6 (67%)	0.335	0.012	0.162

^a Patients with LAM and a history of pneumothorax

^b Patients with AML or PKD and a history of renal procedure

Bold text indicates significant p-values <0.05.

A finding was counted as present if at least one lesion of that type was seen.

Columns show the number of patients with the findings divided by the total number of patients tested, followed by the percent positive in parentheses.

Abbreviations: Sym-AF, Symmetrical-Angiofibroma; Asym-AF, Asymmetrical-Angiofibroma; HM, Hypomelanotic Macule; FCP, Fibrous Cephalic Plaque; SP, Shagreen Patch; Ungual Fibroma, UF; AF, Angiofibroma; DP, Dental Pitting; OF, Oral Fibroma; SEN, Subependymal Nodule; SEGA, Subependymal Giant Cell Astrocytoma; RH, Retinal Hamartoma; LAM, Lymphangioliomyomatosis; AML, Angiomyolipoma; PKD, Polycystic Kidney Disease.

Table S4. Pulmonary Function and Cyst Burden in Patients with LAM and Asymmetrical-Angiofibroma Mosaicism, Symmetrical-Angiofibroma Mosaicism, or Germline Tuberous Sclerosis Complex.

	Germline (G)	Sym-AF Mosaic (Sym)	Asym-AF Mosaic (Asym)	P-values		
				G vs. Sym	G vs. Asym	Sym vs. Asym
%FEV1	98 (22-129) n= 23	92 (36-120) n= 11	87 (47-106) n= 5	<i>0.987</i>	<i>0.586</i>	<i>0.553</i>
%DLCO	87 (16-139) n= 23	84 (51-114) n= 11	88 (50-106) n= 5	<i>0.567</i>	<i>0.559</i>	<i>0.805</i>
Cyst Score	3.8 (0-37) n= 17	5.1 (0-36) n= 10	5.0 (1-18) n= 5	<i>0.809</i>	<i>0.611</i>	<i>0.751</i>

Abbreviations: Sym-AF, Symmetrical-Angiofibroma; Asym-AF, Asymmetrical-Angiofibroma; %FEV1, Forced Expiratory Volume in One Second (% Predicted); %DLCO, Diffusion Capacity of the Lung for Carbon Monoxide (% Predicted).

Data displayed as median (range). Bold text indicates significant p-values <0.05. P-values were determined using t-tests.

Table S5. Age at Onset and Diagnosis for Patients with Asymmetrical-Angiofibroma Mosaicism, Symmetrical-Angiofibroma Mosaicism, or Germline Tuberous Sclerosis Complex.

	Germline (G)	Sym-AF Mosaic (Sym)	Asym-AF Mosaic (Asym)	P-Values		
				G vs. Sym	G vs. Asym	Sym. vs. Asym
1st TSC Finding	0 (0-2) n=28	0 (0-2) n=12	9 (2-15) n=6	<i>0.942</i>	0.042	<i>0.125</i>
TSC Penetrance	4 (2-8) n=27	10 (5-12) n=11	24 (8-34) n=7	0.045	0.043	<i>0.246</i>
TSC Diagnosis	21 (4-31) n=29	19 (13-35) n=12	33 (17-41) n=7	<i>0.621</i>	<i>0.253</i>	<i>0.592</i>
1st Dermatology Visit	37 (31-46) n=29	37 (25-40) n=12	33 (27-41) n=7	<i>0.372</i>	<i>0.236</i>	<i>0.592</i>
LAM Symptom Onset	33 (27-38) n=23	33 (31-34) n=9	26 (24-31) n=5	<i>0.681</i>	<i>0.239</i>	<i>0.364</i>
LAM Diagnosis	36 (31-41) n=23	33 (29-37) n=11	31 (24-35) n=5	<i>0.403</i>	<i>0.215</i>	<i>0.583</i>
1st PFT	37 (33-44) n=23	36 (32-39) n=11	35 (25-46) n=5	<i>0.363</i>	<i>0.413</i>	<i>0.827</i>
AML Diagnosis	30 (25-40) n=24	36 (26-37) n=10	31 (28-35) n=6	<i>0.838</i>	<i>0.667</i>	<i>0.368</i>

Data displayed as median (interquartile range) number of years. Bold text indicates significant p-values <0.05. P-values were determined using Mann-Whitney test.

Abbreviations: Sym-AF, Symmetrical-Angiofibroma; Asym-AF, Asymmetrical-Angiofibroma; TSC, Tuberous Sclerosis Complex; LAM, Lymphangi leiomyomatosis; PFT, Pulmonary Function Testing; AML, Angiomyolipoma.

Table S6. Variant Allele Fraction in Whole and Dissected Tumor Specimens From One Patient with Symmetrical-Angiofibroma Mosaicism (P05).

Specimen	Whole Tumor VAF (%)	Specimen	Epidermis VAF (%)	Dermis VAF (%)
AF1	4.6	AF5	12.4	12
AF2	7.6	AF6	3.6	10.6
AF3	5.3	AF7	1.4	10.9
AF4	5.4	AF8	1.1	9.6

Abbreviations: AF, Angiofibroma; VAF, Variant Allele Fraction.