

## SUPPLEMENTARY DATA:

**Table 1. Rare coding mutations in telomere-maintenance genes identified in the study patients**

Patient	Telomere shortening (percentile)	Chr.	Position <sup>a</sup>	Ref. <sup>b</sup>	Alt. <sup>b</sup>	Gene	rs <sup>c</sup>	CADD score	Frequency in gnomAD	Predicted effect
1	< 1%	X	154005088	AAG	-	DKC1	rs782576893	16.30	0.0038	Codon deletion
2	< 1%	-	-	-	-	-	-	-	-	-
3	< 1%	20	62324564	C	T	RTEL1	rs398123017	37.00	3.208x10 <sup>-5</sup>	Stop gain
4	< 10%	-	-	-	-	-	-	-	-	-
5	< 10%	20	62317210	G	A	RTEL1	rs757365506	14.44	0.0002	Non-synonymous coding
6	< 10%	20	62325833	C	A	RTEL1	rs115610405	16.95	0.0163	Non-synonymous coding
7	< 10%	20	62325833	C	A	RTEL1	rs115610405	16.95	0.0163	Non-synonymous coding
8	< 25%	5	1279520	CGC	-	TERT	-	-	-	Codon deletion
9	< 25%	20	63693247	C	T	RTEL1	rs369419645	19.35	0.00004	Stop gain
10	< 25%	5	1294166	C	T	TERT	rs61748181	8.24	0.0231	Non-synonymous coding
11	< 25%	X	154005088	AAG	-	DKC1	rs782576893	16.30	0.0038	Codon deletion
12	< 25%	5	1254611	A	G	TERT	-	-	-	Non-synonymous coding
13	75-50%	16	14540938	CTG	-	PARN	rs1233589581	-	2.048x10 <sup>-5</sup>	Splice site acceptor

<sup>a</sup>According to human reference genome hg19; <sup>b</sup>Allelic variants found in the reference (Ref.) and in the patient (Alt.); <sup>c</sup>Reference sequence identifier, if available.

**Table 2. Postoperative complications during the first 24 hours after lung transplant**

	All patients (n=20) (%)	With telomere shortening (n=12) (%)	Without telomere shortening (n=8) (%)
Mechanical complications:			
-Phrenic or diaphragmatic paresis	3 (15.0)	1 (8.3)	2 (25.0)
-Atrial tear	1 (5.0)	0 (0.0)	1 (12.5)
-Suture failure	1 (5.0)	1 (8.3)	0 (0.0)
-Hemothorax	1 (5.0)	1 (8.3)	0 (0.0)
Hemodynamic complications:			
-Hemodynamic instability	3 (15.0)	1 (8.3)	2 (25.0)
-Hypovolemic shock	3 (15.0)	3 (25.0)	0 (0.0)
-Distributive shock	1 (5.0)	0 (0.0)	1 (12.5)
Hematological complications:			
-thrombocytopenia	3 (15.0)	3 (25.0)	0 (0.0)
-Coagulation alterations	1 (5.0)	1 (8.3)	0 (0.0)
Primary graft dysfunction	3 (15.0)	2 (16.7)	1 (12.5)
Renal failure	2 (10.0)	1 (8.3)	1 (12.5)
Atrial fibrillation	2 (10.0)	2 (16.7)	0 (0.0)
Donor lung infection	1 (5.0)	0 (0.0)	1 (12.5)
Myopathy of the critical patient	1 (5.0)	1 (8.3)	0 (0.0)

**Table 3. Postoperative complications during the first month after lung transplantation**

	All patients (n=20) (%)	With telomere shortening (n=12) (%)	Without telomere shortening (n=8) (%)
Mechanical complications: -Phrenic or diaphragmatic paresis -Atrial tear -Suture failure	3 (15.0) 1 (5.0) 1 (5.0)	1 (8.3) 0 (0.0) 1 (8.3)	2 (25.0) 1 (12.5) 0 (0.0)
Hemodynamic complications: -Hemodynamic instability -Hypovolemic shock -Distributive shock	3 (15.0) 2 (10.0) 1 (5.0)	1 (8.3) 2 (16.7) 0 (0.0)	2 (25.0) 0 (0.0) 1 (12.5)
Hematological complications: -Plaquetopenia	2 (10.0)	2 (16.7)	0 (0.0)
Primary graft dysfunction	3 (15.0)	2 (16.7)	1 (12.5)
Renal failure	20 (100.0)	12 (100.0)	8 (100.0)
Atrial fibrillation	1 (5.0)	1 (8.3)	0 (0.0)
Donor lung infection	1 (5.0)	0 (0.0)	1 (12.5)
Myopathy of the critical patient	1 (5.0)	1 (8.3)	0 (0.0)

**Table 4. Type of long-term complications after lung transplant**

	All patients (n=19) (%)	With telomere shortening (n=12) (%)	Without telomere shortening (n=8) (%)	P value
Allograft dysfunction Type: -Acute A1-A2 -Acute A2-A3 -Acute A3-A4 -Chronic	8 (42.1) 1 (12.5) 4 (50.0) 2 (25.0) 1 (12.5)	3 (27.3) 1 (33.3) 1 (33.3) 0 (0.0) 1 (33.3)	5 (62.5) 0 (0.0) 3 (60.0) 2 (40.0) 0 (0.0)	0.181 0.286
Renal complications Type: -Renal failure -Ureteral lithiasis + hydronephrosis	7 (35.0) 6 (85.7) 1 (14.3)	4 (33.3) 4 (100) 0 (0.0)	3 (37.5) 2 (66.7) 1 (33.3)	1.000 0.429
Hematological complications Type: -Plaquetopenia -Leukopenia -Anemia	6 (30.0) 4 (66.7) 1 (16.7) 1 (16.7)	4 (33.3) 3 (75.0) 0 (0.0) 1 (25.0)	2 (25.0) 1 (50.0) 1 (50.0) 0 (0.0)	1.000 0.600
Endocrine complications Type: -Diabetes due to corticoids -Dyslipidemia -Cushing Syndrome	15 (75.0) 13 (86.7) 1 (6.67) 1 (6.67)	8 (66.7) 7 (87.5) 1 (12.5) 0 (0.0)	7 (87.5) 6 (85.7) 0 (0.0) 1 (14.3)	0.603 1.000
Infectious complications Type: -Surgical wound infection by <i>S.aureus</i> - <i>P. aeruginosa</i> in BAL -Catheter-related bacteriemia due to <i>S. epidermidis</i> + urinary tract infection due to <i>M. morgani</i> - Catheter-related bacteriemia due to <i>S. epidermidis</i> - Catheter-related bacteriemia due to <i>S. hominis</i> -Urinary tract infection -Endocarditis -Septic thrombophlebitis -Septic shock -Respiratory infection	12 (60.0) 1 (8.3) 1 (8.3) 1 (8.3) 1 (8.3) 1 (8.3) 1 (8.3) 1 (8.3) 1 (8.3) 1 (8.3) 1 (8.3) 2 (16.7) 2 (16.7)	6 (50.0) 1 (16.7) 0 (0.0) 1 (16.7) 1 (16.7) 1 (16.7) 0 (0.0) 1 (16.7) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 2 (33.3)	6 (75.0) 0 (0.0) 1 (16.7) 0 (0.0) 0 (0.0) 1 (16.7) 0 (0.0) 1 (16.7) 0 (0.0) 1 (16.7) 2 (33.3) 0 (0.0)	0.373 0.212
CMV infection - Positive pre-transplant CMV serology - Post-transplant CMV replication - Hematological alterations due to CMV treatment - CMV negativity after treatment	18 (90.0) 14 (73.7) 4 (26.7) 9 (56.2)	11 (91.7) 7 (63.6) 3 (33.3) 4 (44.4)	7 (87.5) 7 (87.5) 1 (16.7) 5 (71.4)	0.338 0.604 0.358

BAL = broncho-alveolar lavage

**Table 5. Post-transplant complications according to family aggregation**

	All patients (n=20)	Patients with family aggregation (n=8)	Patients without family aggregation (n=12)
Presence of telomere shortening [n, %]	12 (60.0)	5 (62.5)	7 (58.3)
Pre-transplant FVC [liters, mean (SD)]	1.87 (0.44)	1.79 (0.31)	1.92 (0.52)
Pre-transplant FVC [%, mean (SD)]	45.3 (11.1)	39.7 (7.6)	49.1 (11.7)
Time from diagnosis to transplantation [months, median((Q1;Q3)]	33.1 (24.0;50.3)	30.1 (21.9;50.3)	33.1 (25.0;46.5)
Postoperative complications in the first 24 hours [n, %]	18 (90.0)	7 (87.5)	11 (91.7)
Extracorporeal circulation need [n,(%)]	4 (20.0)	3 (37.5)	1 (8.33)
Difficult weaning [n,(%)] (n=19)	10 (52.6)	3 (42.9)	7 (58.3)
Tracheostomy [n,(%)] (n=19)	10 (52.6)	3 (42.9)	7 (58.3)
Complications during the first month [n, %] (n=19)	17 (89.5)	6 (85.7)	11 (91.7)
Complications after the first month [n, %] (n=19)	18 (94.7)	6 (85.7)	12 (100.0)
>1 complication after transplantation [n, (%)]* (n=20)	18 (90.0)	6 (75.0)	12 (100.0)
Allograft dysfunction[n, %] (n=19)	8 (42.1)	3 (42.9)	5 (41.7)
Mechanical complications [n, (%)] (n=20)	8 (40.0)	3 (37.5)	5 (41.7)
Nephrological complications [n, %] (n=19)	7 (35.0)	2 (25.0)	5 (41.7)
Hematological complications [n, (%)] (n=20)	6 (30.0)	2 (25.0)	4 (33.3)
Endocrine complications [n, (%)] (n=20)	15 (75.0)	5 (62.5)	10 (83.3)
Infectious complications [n, (%)] (n=20)	12 (60.0)	3 (37.5)	9 (75.0)

Positive pre-transplant CMV serology [n, %]	18 (90.0)	6 (75.0)	12 (100)
Post-transplant CMV replication [n, %] (n=19)	14 (73.7)	5 (71.4)	9 (75.0)
Hematological alterations due to CMV treatment [n, %] (n=15)	4 (26.7)	2 (40.0)	2 (20.0)
CMV negativity after treatment [n, (%)] (n=16)	9 (56.2)	3 (60.0)	6 (54.4)