

CHANGES IN RIGHT HEART HEMODYNAMICS AND ECHOCARDIOGRAPHIC FUNCTION IN AN ADVANCED PHENOTYPE OF PULMONARY HYPERTENSION AND RIGHT HEART DYSFUNCTION ASSOCIATED WITH PULMONARY FIBROSIS

DATA REPOSITORY TABLES

	Patients														
Patient Characteristics	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
NYHA	IV	IV	III	IV	III	III	III	IV	III	IV	IV	III	IV	III	III
Age in Years (at study entry)	69	75	67	84	60	44	40	71	34	68	71	65	65	65	69
Background Therapy	P	E/P	E	N	E	P	P	E/P	P	N	E/P	N	N	N	N
Clinical Subtype	IPF	IPF	IPF	IPF	NSIP-F	S	NSIP-F	CPFE	HP	CPFE	IPF	CPFE	IPF	IPF	IPF
Treprostinil dose at discharge	2	1	2	3	5	6	2	6	2	4	2	2	2	2	2
Treprostinil dose at 3 months	33	19	32	18	32	17	30	23	25	19	36	18	25	38	50
Treprostinil dose at 6 months	32	19	-	18	52	17	34	42	30	27	29	80	36	38	-
Treprostinil dose at 12 months	-	19	-	-	52	17	34	-	30	27	-	-	36	41	-
Treprostinil dose at last visit (i.e at time of lung transplant or at last clinic visit just before death)	36	19	32	18	52	17	34	55	29	16	29	80	56	26	58
Outcome	T	D	T	D	T	T	A	D	T	D	D	D	A	T	T
Time from treatment initiation to Outcome/Censor (days)	257	858	118	199	267	348	1498	311	1255	576	275	272	1351	606	148

**Table 1:** Patient demographics, underlying fibrotic lung disease clinical subtype, and background PH-targeted therapy

Background Endothelin receptor antagonist (E); Phosphodiesterase 5 inhibitor (P); No background therapy (N)

Clinical Subtypes: Idiopathic Pulmonary Fibrosis (IPF); NSIP-Fibrosis (NSIP-F); PF/Emphysema (CPFE); Chronic Hypersensitivity Pneumonitis (HP); Silicosis (S)

Outcome: Transplant (T); Death (D); Alive/Censor (A)

	Patients														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Pathologic Confirmation	Y	Y	Y	N	Y	Y	Y	N	Y	N	N	N	Y	Y	Y
< or > 20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%
Total Combined Score	5	4	3	3	5	3	3	3	5	3	5	4	4	5	4
Total Fibrosis RT Lung	2	4	2	3	2	1	1	3	3	2	1	3	3	3	2
Total Fibrosis LT Lung	2	4	2	3	2	1	1	3	3	2	0	3	3	3	2
Fibrosis RT Upper Lobe	1	3	2	2	2	1	1	2	3	1	0	2	2	3	2
Fibrosis RT Middle Lobe	2	3	2	2	3	1	1	2	3	1	1	3	3	3	2
Fibrosis RT Lower Lobe	2	4	1	3	3	1	1	3	3	2	0	3	4	3	1
Fibrosis LT Upper Lobe	1	3	2	2	2	1	1	2	3	1	0	2	2	3	2
Fibrosis LT Lower Lobe	2	4	1	3	3	1	1	3	3	2	0	3	4	3	2
Total GGO RT Lung	4	2	1	2	4	2	1	0	2	2	1	1	2	1	0
Total GGO LT Lung	4	1	1	2	4	2	1	0	2	2	0	1	2	1	0
GGO RT Upper Lobe	4	1	1	2	4	2	1	0	2	1	1	1	3	1	0
GGO RT Middle Lobe	4	1	1	2	4	2	1	0	2	1	1	1	2	1	0
GGO RT Lower Lobe	4	2	1	2	4	2	1	0	2	2	0	1	1	1	0
GGO LT Upper Lobe	4	2	1	2	4	2	1	0	2	1	0	1	2	1	0
GGO LT Lower Lobe	4	2	1	2	4	2	1	0	2	2	0	1	1	1	0
Total HC RT Lung	1	1	0	2	0	0	3	1	0	0	4	2	0	2	3
Total HC LT Lung	0	1	0	2	0	0	3	1	0	0	5	2	0	2	2
HC RT Upper Lobe	0	1	0	2	0	0	2	1	0	0	3	1	0	3	1
HC RT Middle Lobe	0	1	0	1	0	0	3	1	0	0	2	2	0	1	2
HC RT Lower Lobe	1	1	0	2	0	0	4	1	0	0	5	2	0	1	3
HC LT Upper Lobe	0	1	0	2	0	0	2	1	0	0	5	2	0	2	1
HC LT Lower Lobe	0	1	0	2	0	0	4	1	0	0	5	2	0	1	3

Table 2: Baseline high resolution computed tomography (HRCT) analysis of lung parenchymal abnormalities  
RT: Right; LT: Left; GGO: Ground Glass Opacity; HC: Honeycombing; Ordinal Scoring System for Degree of Radiographic Involvement: 0= None; 1= 1 to 5%; 2= 6 to 25%; 3= 25 to 50%; 4= 51 to 75%; 5= >75%

	Week	Patients														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
<u>Pulmonary Function</u>																
FVC, % Predicted	0	57	38	78	54	69	57	50	88	58	77	37	105	84	44	38
	12	66	33	82	62	74	64	54	66	63	82	38	94	84	44	41
FEV <sub>1</sub> , % Predicted	0	58	48	74	70	74	43	51	90	49	71	43	95	70	46	49
	12	71	43	80	75	80	52	55	76	54	79	43	90	70	44	53
FEV <sub>1</sub> /FVC	0	-	93	70	91	85	59	82	75	70	68	84	67	64	79	87
	12	81	96	73	85	109	65	82	85	70	71	82	71	64	76	88
TLC, % Predicted	0	71	45	78	58	51	89	64	78	75	84	59	98	84	55	55
	12	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
DLCO, % Predicted	0	24	31	34	12	15	61	28	9	27	26	15	26	18	17	16
	12	29	-	-	14	19	61	33	22	23	29	12	22	18	14	25
FVC%/DLCO%	0	2.4	1.2	2.3	4.5	4.6	0.9	1.8	9.8	2.1	3	2.5	4	4.7	2.6	2.4
	12	2.3	-	-	4.4	3.9	1	1.6	3	2.7	2.8	3.2	4.3	4.7	3.1	1.6
Oxygen Flow (Liters/min)	0	2	5	3	6	6	4	0	5	3	3	6	2	6	5	2
	12	2	4	3.5	6	6	6	0	4	2.5	1	7	3	6	5	2
	26	2	4	-	6	6	8	3	4	2.5	3	8	6	6	5	-
	52	-	5	-	-	-	-	3	-	2	4	-	-	-	4	-
<u>Six Minute Walk:</u>																
6-minute walk distance (meters)	0	93	190	330	1	159	120	324	78	210	210	90	210	210	90	255
	12	240	180	390	18	216	150	414	99	360	303	120	200	327	160	275
	26	235	178	-	0	126	190	420	75	363	272	80	291	240	142	-
	52	-	165	-	-	-	-	507	-	333	275	-	-		80	-
Room Air % saturation (RA)	0	-	87	84	79	79	90	82	84	94	84	66	85	80	74	89
	12	-	85	79	78	65	86	92	80	94	84	61	88	79	64	80
10L face mask, % saturation	0	97	98	97	100	95	98	100	100	99	97	100	99	98	92	100
	12	100	94	95	96	100	97	100	99	100	98	99	100	97	86	100
10L face mask, % saturation nadir	0	93	75	76	89	81	97	92	80	98	82	77	87	85	70	95
	12	-	80	76	89	72	91	87	86	96	86	70	89	72	60	88
<u>BDI Score</u>	0	-	-	-	-	13	9	14	12	16	17	17	13	13	14	13
	12	-	17	13	13	13	9	14	13	13	17	15	11	13	8	15

Table 3: Pulmonary function testing, oxygen requirements, and 6 minute walk distance with Borg dyspnea index scores at baseline and end of study

	Week	Patients														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
<u>Quality of Life/Dyspnea</u>																
UCSD SOB	0	97	63	54	103	81	-	89	115	100	101	94	76	79	-	79
	12	67	77	32	101	70	-	68	104	71	88	72	43	52	97	81
SF36 PCS aggregate	0	-	15	87	33	56	21	52	.	17	16	22	40.4	20.2	13.2	63
	12	-	38	97	17	17	61	54	9	82	65	86	59.4	24.4	45.2	68
SF36 MCS aggregate	0	-	58	129	28	64	31	50	.	68	27	67	37.9	43.97	48.27	108.37
	12	-	80	137	48	112	42	74	63	108	72	79	73.63	56.53	68.53	106.3
<u>Individual SF36 Domains</u>																
Physical Functioning	0	-	10	25	0	0	0	25	-	15	0	0	15	10	0	20
	12	-	25	35	0	0	100	30	0	45	15	15	50	5	15	30
Role-Physical	0	-	0	200	0	100	0	125	-	0	0	0	25	0	0	100
	12	-	100	300	0	0	100	125	0	200	200	275	100	0	100	100
Bodily Pain	0	-	32	100	100	100	52	52	-	41	42	62	62	61	31	100
	12	-	12	52	32	31	50	41	22	74	31	62	52	62	41	100
General Health	0	-	10	52	45	45	20	30	-	10	25	20	45	0	10	25
	12	-	25	42	35	25	10	30	5	25	40	30	40	15	25	40
Vitality	0	-	25	60	20	35	35	30	-	20	15	30	55	30	25	70
	12	-	30	55	20	30	45	45	20	65	40	50	55	40	45	70
Social Functioning	0	-	63	88	13	25	38	38	-	25	0	38	37.5	12.5	25	37.5
	12	-	75	100	13	38	0	63	0	88	25	63	62.5	25	50	37.5
Role-Emotional	0	-	133	367	0	133	0	100	-	233	67	200	0	133.33	133.33	333.33
	12	-	200	400	100	400	100	167	233	300	200	200	166.67	166.67	166.67	300
Mental Health	0	-	60	80	64	84	64	52	-	52	28	48	52	44	48	76
	12	-	68	88	72	68	56	64	56	60	56	52	44	36	56	84

Table 4: Quality of life and dyspnea score changes using Short Form 36 (SF-36) and University of California San Diego shortness of breath questionnaire  
 PCS: Physical Component Summary; MCS: Mental Component Summary

	Week	Patients														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
<u>Hemodynamic s. mmHg</u>																
Right atrial pressure (RA)	0	11	12	18	8	8	9	8	14	11	7	6	10	10	5	6
	12	5	9	11	1	8	11	0	8	9	4	6	8	2	2	3
mean Pulmonary Pressure (mPA)	0	49	56	59	40	50	55	46	53	52	40	56	42	36	38	36
	12	20	51	51	30	48	70	29	49	35	31	47	35	22	32	34
Pulmonary Artery Wedge Pressure	0	18	12	18	6	10	15	15	5	14	10	9	12	14	18	11
	12	10	25	15	7	9	20	4	7	15	6	12	8	4	10	5
Cardiac Output (L/min)	0	3.73	3.75	3.87	3	4.1	3.07	7.2	2.9	5	3.7	4.5	5	5.7	4.6	3.6
	12	4	5.5	6.23	2.8	5.5	4.2	5.9	4.2	5.9	3.9	3.3	6.2	5.1	5.7	4.5
Cardiac Index (L/min/m <sup>2</sup> )	0	2.2	2.25	2.02	1.75	2.3	1.68	3.36	1.31	2.7	1.96	2.6	2.8	3.05	2.2	2.1
	12	2.63	3.35	3.31	1.6	3.13	2.28	2.75	2.28	3.17	2.16	1.92	3.46	2.8	3.54	2.6
PVR (dyn sec/cm <sup>5</sup> )	0	600	874	786	906	784	1040	344	1324	608	649	835	480	336	347	555
	12	200	378	462	657	567	952	338	800	271	512	848	348	282	313	515
Mixed Venous O <sub>2</sub> Saturation (%)	0	60	61	65	60	72	69	-	49	-	65	75	69	.	69	.
	12	66	68	77	69	79	58	-	59	76	79	72	80	.	72	66
Hemoglobin (g/dL)	0	10.1	12.8	17.1	14.5	12.5	16.1	16.4	13	17.3	15	11.2	14	12.5	14.5	13.8
	12	10.8	13	16.5	13.8	13.1	12.9	14.9	11.3	14.6	18.7	10.1	15	12.9	14.4	11.8
Arterial O <sub>2</sub> Content (mL O <sub>2</sub> /100mL)	0	-	1547.9	1996.6	1592.25	1372.63	2014.11	1869.27	1517.88	2260.42	1751.4	1027.49	1654.1	1390	1491.47	1707.2
	12	-	1535.95	1811.87	1496.2	1183.59	1542.07	1905.41	1256.56	1907.64	2183.41	856.38	1834.8	1416.55	1281.02	1312.16
O <sub>2</sub> Delivery (mL/min)	0	-	5804.64	7726.83	4776.74	5627.76	6183.32	13458.8	4401.85	11302.1	6480.18	4623.7	8270.5	7923	6860.76	6145.91
	12	-	8447.73	11287.9	4189.35	6509.72	6476.68	11241.9	5277.55	11255.1	8515.31	2826.05	11375.8	7224.4	7301.84	5904.72
Pulmonary Capacitance (mL/mmHg)	0	1.15	1.25	1.06	0.87	1.06	0.56	2.5	0.96	1.09	1.27	0.85	1.79	2.06	1.6	1.51
	12	3.03	1.34	1.84	1.17	1.16	0.63	3.29	1	2.45	1.54	0.62	1.75	3.8	1.78	1.6
RV Pulsatility	0	0.92	0.71	0.78	1.35	0.98	1.07	0.87	0.85	0.92	0.9	1.07	0.74	0.92	1.05	0.97
	12	1	0.902	0.9216	1.4	1.125	0.9714	0.9655	1.0204	0.8286	1.0323	1.234	1.0571	0.7727	1.25	1.0588
Pulse Pressure	0	45	40	46	54	49	59	40	45	48	36	60	31	33	40	35
	12	20	46	47	42	54	68	28	50	29	32	58	37	17	40	36
Stroke Volume (mL)	0	51.81	50	48.99	46.88	51.9	33.01	100	43.28	52.08	45.68	51.14	55.56	67.86	63.89	52.94
	12	60.61	61.8	86.53	49.12	62.5	42.86	92.19	50	71.08	49.37	35.87	64.58	64.56	71.25	57.69
Stroke Volume Index	0	30.56	30	25.57	27.34	29.11	18.06	46.67	19.55	28.13	24.2	29.55	31.11	36.31	30.56	30.96
	12	35.75	37.08	45.16	28.66	35.06	23.45	43.02	22.59	38.39	26.15	20.72	36.17	34.54	34.08	33.74
Systolic Blood Pressure	0	125	160	124	136	109	119	-	90	128	135	159	110	135	91	120
	12	107	147	101	103	106	113	-	100	126	109	127	105	108	118	116
Mean Arterial Pressure	0	75	114	91	98	68	96	-	70	92	105	113	83	92	73	70
	12	81	108	87	75	76	90	-	82	94	85	94	75	75	81	84
HR (beats/minute)	0	72	75	79	64	79	93	72	67	96	81	88	90	84	72	68
	12	66	89	72	57	88	98	64	84	83	79	92	96	79	80	78
Rs (dyn sec/cm <sup>5</sup> )	0	1222.52	2176	1509.04	2453.33	1131.71	2110.75	-	1793.1	1248	2054.05	1848.89	1136	1094.74	956.52	1311.11
	12	1420	1207.27	924.56	1942.86	974.55	1333.33	-	1428.57	1071.19	1620.51	1987.88	864.52	1113.73	996.49	1404.44
PVR/Rs	0	0.49	0.4	0.52	0.37	0.69	0.49	-	0.74	0.49	0.32	0.45	0.42	0.31	0.36	0.42
	12	0.14	0.31	0.5	0.34	0.58	0.71	-	0.56	0.25	0.32	0.43	0.4	0.25	0.31	0.37
TPG	0	31	44	41	34	40	40	31	48	38	30	47	30	22	20	25

	12	10	26	36	23	39	50	25	42	20	25	35	27	18	22	29
BNP (pg/mL)	0	352	368	858	839	171	125	21	3470	20	66	250	408	54	554	810
	12	150	31	644	288	77	213	20	1310	20	123	20	102	20	165	244
	26	84	64	-	251	165	113	20	2030	20	20	240	189	21	102	-
	52	-	39	-	-	-	-	20	-	20	81	-	-	-	607	-

Table 5: Systemic & pulmonary hemodynamics and oxygenation at baseline compared to 12 weeks after parenteral treprostinil therapy

PVR: pulmonary vascular resistance; pulmonary capacitance = (stroke Volume/pulse pressure); Rs: systemic vascular resistance

TPG: transpulmonary gradient)

BNP: brain natriuretic peptide