

Data Supplement

SILDENAFIL TO IMPROVE RESPIRATORY REHABILITATION OUTCOMES IN COPD: A CONTROLLED TRIAL

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Supplementary Table 1

Baseline characteristics of subjects screened with Doppler echocardiography and evaluated with right heart catheterisation

	Patients screened with Doppler echocardiography n=49	Patients evaluated with right heart catheterisation n=14	p-value
Gender, male (%)	43 (88%)	13 (93%)	1.000
Age, years	69 (61, 71)	59 (55, 65)	0.006
Body mass index (kg/m ²)	25.6 (23.1, 28.4)	28.6 (24.1, 31.9)	0.180
Forced vital capacity (FVC), % predicted	66 (59, 76)	63 (50, 78)	0.645
Forced expiratory volume in the first second (FEV ₁), % predicted	30 (24, 35)	33 (22, 45)	0.494
Total lung capacity, % predicted	115 (105, 129)	110 (100, 119)	0.213
Diffusing capacity for carbon monoxide, % predicted	38 (32, 49)	41 (23, 47)	0.974
Partial pressure of arterial oxygen, mmHg	69 (56, 77)	63 (58, 72)	0.720
Systolic pulmonary artery pressure, mmHg ^a	41 (37, 46)	36 (34, 40)	0.693
Endurance time ^b , seconds	230 (172, 341)	260 (203, 331)	0.527
Maximal exercise tolerance ^c , watts	35.0 (23, 44)	26.5 (18, 43)	0.086
Oxygen consumption at peak exercise ^c , mL/min	733 (633, 916)	863 (596, 1101)	0.316
Six-minute walk distance, meters	376 (330, 435)	403 (360, 455)	0.475
SGRQ Total score	50.3 (40.1, 65.4)	60.4 (36.9, 66.3)	0.446

^a Estimated from maximum tricuspid regurgitation velocity measured at Doppler echocardiography, assuming a right atrial systolic pressure of 5 mmHg.

^b In the constant work-rate exercise test

^c: In the incremental cardiopulmonary exercise test

Values are given as median (percentile 25, percentile 75) or n (%).

Supplementary Table 2**Characteristics of the subjects who were studied by right heart catheterisation (baseline)**

	Sildenafil n=9	Placebo n=5	p-value
Gender, male (%)	8 (89%)	5 (100%)	
Age, years	60 (55, 65)	58 (56, 60)	0.8425
Body mass index (kg/m ²)	28.2 (23.7, 30.1)	29.1 (26.3, 31.9)	0.696
Forced vital capacity (FVC), % predicted	61 (44, 78)	71 (56, 74)	0.558
Forced expiratory volume in the first second (FEV ₁), % predicted	27 (22, 45)	37 (32, 44)	0.558
FEV ₁ /FVC	0.46 (0.33, 0.47)	0.40 (0.33, 0.51)	1.000
Total lung capacity, % predicted	108 (100, 117)	117 (105, 122)	0.648
Diffusing capacity for carbon monoxide, % predicted	38 (23, 46)	43 (42, 47)	0.251
Partial pressure of arterial oxygen, mmHg	62 (58, 67)	64 (63, 72)	0.794
Mean pulmonary artery pressure, mmHg	31 (29, 33)	26 (26, 27)	0.0834
Mean pulmonary capillary wedge pressure, mmHg	9 (6, 13)	13 (11, 13)	0.558
Mean right atrial pressure, mmHg	5 (5, 8)	6 (5, 6)	1.000
Cardiac index, L/min/m ²	2.53 (2.39, 3.17)	2.98 (2.4, 3.05)	1.000
Endurance time ^a , seconds	268 (203, 307)	252 (221, 460)	0.517
Maximal exercise tolerance ^b , watts	18 (18, 32)	29 (28, 33)	0.203
Oxygen consumption at peak exercise ^b , mL/min	40 (32, 47)	41 (41, 49)	0.334
Six-minute walk distance, meters	374 (359, 400)	455 (408, 485)	0.041
SGRQ Total score	61.2 (51.5, 66.3)	59.6 (36.9, 63.3)	0.896

^a: In the constant work-rate exercise test

^b: In the incremental cardiopulmonary exercise test

Values are given as median (percentile 25, percentile 75) or n (%)

Supplementary Table 3

Effects of sildenafil in combination with pulmonary rehabilitation on efficacy outcomes in subjects studied by right heart catheterisation

		Baseline	Change from baseline	Sildenafil - Placebo Change differences
Primary outcome				
Endurance time ^a , seconds	Sildenafil	268 [175 to 331]	149 [51 to 589]	-241 [-1132 to 277]
	Placebo	252 [188 to 546]	485 [0 to 1650]	
Secondary outcomes				
Maximal exercise tolerance ^b , watts	Sildenafil	29 [13 to 59]	7 [-2 to 12]	0 [-10 to 18]
	Placebo	46 [40 to 71]	4 [-2 to 28]	
Oxygen consumption at peak exercise ^b , mL/min	Sildenafil	844 [423 to 1169]	82 [-57 to 249]	95 [-96 to 306]
	Placebo	924 [841 to 1110]	-57 [-59 to 330]	
Six-minute walk distance, meters	Sildenafil	374 [325 to 437]	31 [-12 to 51]	10 [-43 to 33]
	Placebo	455 [406 to 495]	21 [-12 to 34]	
SGRQ Total score	Sildenafil	61.2 [32.66 to 77.75]	-3.98 [-14.31 to 19.18]	0.2 [-19.58 to 19.84]
	Placebo	59.6 [32.52 to 81.58]	-2.42 [-12.44 to 0.67]	
SF-36 Aggregate physical score	Sildenafil	20.0 [5.0 to 25.0]	12.5 [0.0 to 70.0]	7.5 [-10.0 to 55.0]
	Placebo	55.0 [15.0 to 65.0]	7.5 [-5.0 to 15.0]	
SF-36 Aggregate mental score	Sildenafil	72.0 [16.0 to 76.0]	0.0 [-12.0 to 36.0]	-8 [-48.0 to 36.0]
	Placebo	68.0 [36.0 to 100.0]	10.0 [-24.0 to 40.0]	

Values are median and [95% CI]. Sample sizes are n=9 and n=5 for Sildenafil and Placebo, respectively. Results are based on the imputed data using the 10th percentile to impute, except for SGRQ where the 90th percentile was used instead.

^a: In the constant work-rate exercise test

^b: In the incremental cardiopulmonary exercise test

Definition of abbreviations: SGRQ: St George Respiratory Questionnaire; SF-36: Medical Outcomes Study 36-Item Short Form Health Survey.