

Supplementary table 1A. Hemodynamic values for PAH patients

		All patients	CTD-PAH	IPAH/HPAH	Initial combination therapy	Initial monotherapy
Sample size (% females)		21 (71)	8 (100)	13 (54)	5 (80)	16 (69)
Age (years)		70 (57 - 75)	70 (62 - 73)	72 (57-75)	55 (45 - 70)	72 (66 - 77)
BSA (m ²)		1.78 (1.7 - 2.08)	1.72 (1.69 - 1.77)	1.89 (1.77 - 2.17)	1.78 (1.66 - 2.08)	1.78 (1.7 - 2.05)
MPAP (mmHg)	B	45 (39 - 55)	41.5 (38.8 - 44.3)	50 (42 - 55)	56 (50 - 57)	43.5 (38.8 - 49.8)
MPAP (mmHg)	C1	40 (34 - 48)	36 (33.5 - 42)	41 (35 - 48)	48 (42 - 48)	39 (34 - 42.8)
MPAP (mmHg)	C2	39 (34 - 44) ‡	39 (35.5 - 43)	37 (30 - 44) ‡	39 (39 - 41)	36.5 (30 - 44.5) ‡
PAWP (mmHg)	B	6 (5 - 7)	6 (5 - 6.3)	6 (5 - 7)	6 (6 - 7)	6 (5 - 6.3)
PAWP (mmHg)	C1	6 (5 - 10)	5.5 (4.8 - 9)	6 (5 - 10)	6 (5 - 7)	6 (4.8 - 10)
PAWP (mmHg)	C2	6 (5 - 9)	7 (6 - 8.3)	5 (5 - 9)	5 (5 - 6)	7 (5 - 9.3)
MRAP (mmHg)	B	7 (6 - 9)	7 (6 - 10)	7 (4 - 9)	9 (7 - 11)	6 (4 - 8.3)
MRAP (mmHg)	C1	6 (4 - 10)	8.5 (5.8 - 11)	4 (3 - 8)	6 (6 - 11)	6 (3.8 - 9.3)
MRAP (mmHg)	C2	4 (4 - 8)	11 (6.3 - 15)	4 (2 - 6) ‡	4 (4 - 8)	5 (3.5 - 8.5)
CO (l·min ⁻¹)	B	3.6 (3 - 4.6)	3.6 (3.1 - 4.7)	3.6 (3 - 4.4)	3 (2.9 - 3)	3.9 (3.4 - 4.9) *
CO (l·min ⁻¹)	C1	4.5 (3.5 - 5.7) ‡	4.7 (3.5 - 5.2) ‡	4.5 (3.5 - 5.7) ‡	3.6 (3.5 - 5)	4.7 (3.6 - 5.8) ‡
CO (l·min ⁻¹)	C2	4.2 (3.5 - 4.9) ‡	3.8 (3.3 - 4.5)	4.8 (3.7 - 5.9) ‡	3.8 (3.5 - 3.8) ‡	4.6 (3.7 - 5.1)
PVR (WU)	B	10.2 (7.9 - 12.4)	8.9 (7.2 - 11)	11.9 (8.2 - 14.5)	16.9 (14.9 - 17.2)	8.8 (7.3 - 11.3) *
PVR (WU)	C1	7.5 (5.8 - 9.3) ‡	7.3 (5.7 - 8.9) ‡	7.5 (6.5 - 9.6) ‡	10.4 (6.5 - 12.2)	7.1 (5.8 - 8.8) ‡
PVR (WU)	C2	7.8 (6 - 8.9) ‡	8.3 (6 - 8.9)	6.9 (6.3 - 8.9) ‡	8.9 (8.7 - 9.1) ‡	6.7 (6 - 8.7) ‡
SVR (WU)	B	25.4 (18.3 - 28.3)	23.1 (17.7 - 25.9)	26 (19.8 - 32.4)	26.7 (26 - 32.4)	23.6 (17.2 - 27.1)
SVR (WU)	C1	16.9 (13 - 24.8) ‡	16.8 (12.7 - 19.8) ‡	18.9 (13.8 - 25.7) ‡	19.2 (13 - 25.7) ‡	16.8 (13.6 - 22.3) ‡
SVR (WU)	C2	16.3 (14.7 - 21.4) ‡	19.6 (15.3 - 22.1)	16 (14.7 - 20) ‡	21.6 (14.7 - 24.9)	16.2 (15.3 - 20.2) ‡
RVSWI (mmHg·ml·m ⁻²)	B	921.7 (800.6 - 1137.7)	853.9 (799.2 - 975.7)	1001.6 (800.6 - 1211.2)	800.6 (776.8 - 898.9)	1005.9 (808.4 - 1230.5)
RVSWI (mmHg·ml·m ⁻²)	C1	1065.4 (961.4 - 1330.8)	977.3 (849.4 - 1349.4)	1083.6 (962.8 - 1305.4)	978.5 (976 - 1058.6)	1169.6 (861.8 - 1365.2)
RVSWI (mmHg·ml·m ⁻²)	C2	995.2 (693.9 - 1254.6)	729.3 (597.7 - 1026.8)	1203.3 (920 - 1288.5)	1203.3 (963.6 - 1206.7)	957.6 (597.7 - 1370.2)
LVSWI (mmHg·ml·m ⁻²)	B	2159.4 (1969.7 - 2600.7)	2133.1 (1919.7 - 2755)	2175.7 (1969.7 - 2600.7)	1635.3 (1598.5 - 1863)	2429.3 (2114 - 2938.8) *
LVSWI (mmHg·ml·m ⁻²)	C1	2581.2 (2155.7 - 2835.6)	2529.3 (2068.8 - 2716.8)	2617.2 (2407.7 - 2858.3)	2477.5 (2407.7 - 2556.5)	2665 (2139.4 - 2918.6)
LVSWI (mmHg·ml·m ⁻²)	C2	2548.4 (2104.7 - 3122.7) ‡	2107 (2085.6 - 2940.1)	2573.5 (2231.2 - 3155.3)	2573.5 (2104.7 - 2819.2)	2475.4 (2104.6 - 3130.9)

Continuous variables are presented as median (interquartile range). Baseline values significantly different between initial combination versus monotherapy groups are marked by a *. ‡ notes a significant difference between the marked value and the baseline value for the addressed parameter and group. B, baseline; C1, first checkup; C2, second checkup; CTD-PAH, connective tissue disease pulmonary arterial hypertension; HPAH, hereditary pulmonary arterial hypertension; IPAH, idiopathic pulmonary arterial hypertension; MPAP, mean pulmonary arterial pressure; MRAP, mean right atrial pressure; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; RVSWI, right ventricular stroke work index; SVR, systemic vascular resistance; WU, wood unit.

Supplementary table 1B. WHO-FC, 6MWD and NT-proBNP values for PAH patients.

		All patients	CTD-PAH	IPAH/HPAH	Initial combination therapy	Initial monotherapy
Sample size (% females)		21 (71)	8 (100)	13 (54)	5 (80)	16 (69)
WHO-FC	B	3 (3 - 3)	3 (3 - 3)	3 (3 - 3)	3 (3 - 3)	3 (3 - 3)
WHO-FC	C1	3 (2 - 3)	3 (3 - 3)	3 (2 - 3)	2 (2 - 3)	3 (3 - 3)
WHO-FC	C2	3 (3 - 3)	3 (3 - 3)	3 (2 - 3)	3 (2 - 3)	3 (3 - 3)
6MWD (m)	B	213.5 (142.5 - 258.5)	207 (157.5 - 251)	220 (162.5 - 260)	241.5 (213.8 - 278.5)	203.5 (121.3 - 243.5)
6MWD (m)	C1	240 (168.5 - 310)	187 (151 - 263)	255 (200 - 345)	302 (274.5 - 344.8)	208.5 (143.3 - 270)
6MWD (m)	C2	224 (150 - 371.3) ‡	150 (123 - 200.5)	275 (175 - 375) ‡	367.5 (302.5 - 408.8)	176.5 (150 - 273.8)
NT-proBNP (ng/l)	B	2359 (1666.5 - 3088.5)	3259.5 (2603.8 - 4089.3)	1689 (843 - 2359) †	2634.5 (2338.8 - 2977.8)	2325 (1243.5 - 3088.5)
NT-proBNP (ng/l)	C1	1455 (642 - 2468.5) ‡	2468.5 (1658.8 - 3532.5)	707 (391 - 1054)	1133.5 (674.5 - 1915.5)	1455 (619 - 2835.5)
NT-proBNP (ng/l)	C2	958 (420.5 - 3264.5) ‡	3264.5 (2597.8 - 5147)	541 (140 - 958) ‡	2104.5 (753.5 - 3257.8)	700 (420.5 - 3012.5)

Continuous variables are presented as median (interquartile range). Baseline values significantly different between CTD-PAH versus IPAH are marked by a †. ‡ notes a significant difference between the marked value and the baseline value for the addressed parameter and group. WHO-FC is used for descriptive purposes. B, baseline; C1, first checkup; C2, second checkup; 6MWD, 6 minute walk distance; CTD-PAH, connective tissue disease pulmonary arterial hypertension; HPAH, hereditary pulmonary arterial hypertension; IPAH, idiopathic pulmonary arterial hypertension; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; WHO-FC, World Health Organization functional class.

Supplementary table 1C. Biomarker values for PAH patients.

		All patients	CTD-PAH	IPAH/HPAH	Initial combination therapy	Initial monotherapy
Sample size (% females)		21 (71)	8 (100)	13 (54)	5 (80)	16 (69)
FGF-2 (pg/ml)	B	15.16 (10.75 - 20.64)	14.02 (9.99 - 14.43)	17.89 (13.49 - 26.11)	17.47 (14.18 - 18.65)	14.66 (10.1 - 23.48)
FGF-2 (pg/ml)	C1	14.37 (7.19 - 29.09)	8.99 (7.77 - 17.45)	24.3 (7.19 - 41.17)	16.87 (7.99 - 28.38)	12.09 (7.17 - 31.53)
FGF-2 (pg/ml)	C2	15.75 (7.53 - 21.92)	17.81 (13.41 - 20.58)	14.1 (7.23 - 43.07)	5.84 (5.05 - 7.53)	17.81 (13.18 - 43.74)
PIGF (pg/ml)	B	31.02 (21.74 - 38.14)	39.22 (30.93 - 44.85)	30.44 (21.07 - 32.68)	30.66 (18.09 - 32.68)	31.45 (26.86 - 39.58)
PIGF (pg/ml)	C1	34.64 (26.38 - 40.94)	40.61 (32.41 - 43.72)	27.65 (21.67 - 37.2)	27.65 (20.06 - 28.33)	35.94 (26.51 - 42.72)
PIGF (pg/ml)	C2	30.96 (26.52 - 36.8)	37.62 (32.9 - 39.62)	28 (24.01 - 32.14)	28.56 (26.52 - 39.48)	31.55 (27.32 - 36.49)
sFlt-1 (pg/ml)	B	124 (95.2 - 148.9)	125.9 (92 - 330.5)	124 (103.6 - 144.2)	188 (130.6 - 214.1)	119.3 (89.2 - 138.7)
sFlt-1 (pg/ml)	C1	110.2 (79.9 - 127.7) ‡	103 (73.8 - 145) ‡	110.2 (99 - 127.3)	99 (79.9 - 141.4) ‡	112.2 (84 - 127.4)
sFlt-1 (pg/ml)	C2	93.7 (79.2 - 116) ‡	108.8 (82.1 - 141.4)	88.5 (78.2 - 104.4) ‡	80.6 (79.2 - 132)	94.5 (81.8 - 115) ‡
Tie-2 (pg/ml)	B	3284.8 (2818.9 - 3607.4)	2832.5 (2741.4 - 3168.7)	3415.9 (2984 - 3769.6)	3284.8 (3110.3 - 3415.9)	3163.9 (2813.1 - 3695.7)
Tie-2 (pg/ml)	C1	3118.3 (2727.3 - 3427.9)	2787.4 (2543.8 - 3103.6)	3234.5 (3102 - 3450.9)	3222.1 (2694.3 - 3415.7)	3110.1 (2764.8 - 3449.6)
Tie-2 (pg/ml)	C2	3436.2 (2983.5 - 3676.4)	3076.5 (2657.8 - 3303.3)	3641.5 (3092.7 - 3850.4)	3502.6 (2889.3 - 3621.1)	3347.6 (3036.9 - 3718.7)
VEGF-A (pg/ml)	B	81 (73.6 - 150.4)	133.9 (79.8 - 222.5)	74.4 (62.5 - 131.2)	74.3 (73.6 - 79.9)	122.7 (72.7 - 155.1)
VEGF-A (pg/ml)	C1	96.6 (69.4 - 170.3)	148 (104.8 - 189.3)	69.8 (59.3 - 112)	112 (53.5 - 151.2)	94.2 (69.7 - 189.3)
VEGF-A (pg/ml)	C2	92.8 (59.9 - 176.2)	119.3 (92.4 - 233.1)	79.5 (50.4 - 120.9)	79.5 (40.8 - 92.8)	109 (68.6 - 176.5)
VEGF-D (pg/ml)	B	1222.8 (801.5 - 1322.7)	1351.7 (1224.8 - 1482)	905.8 (712.5 - 1230.5) †	1222.8 (690.3 - 1232.4)	1216.3 (853.2 - 1357.8)
VEGF-D (pg/ml)	C1	1098.8 (821.5 - 1324.6)	1239.9 (1060.6 - 1824.8)	1007.1 (789.1 - 1227.4)	969.7 (835 - 1007.1)	1215.1 (814.8 - 1363.5)
VEGF-D (pg/ml)	C2	1060.5 (722.1 - 1437.1)	1569.2 (989.4 - 1943.8)	976.8 (624.6 - 1169.2)	1036.3 (722.1 - 1161.7)	1114.9 (782.2 - 1466.6)
IL-6 (pg/ml)	B	1.58 (0.9 - 3.8)	2.3 (1.42 - 3.67)	1.37 (0.86 - 3.8)	1.47 (0.9 - 1.85)	1.69 (1 - 3.84)
IL-6 (pg/ml)	C1	1.3 (0.57 - 2.33) ‡	1.39 (0.8 - 2.37)	0.88 (0.52 - 2.14) ‡	0.73 (0.57 - 1.31)	1.34 (0.66 - 2.33) ‡
IL-6 (pg/ml)	C2	1.56 (0.74 - 2.01)	1.79 (1.01 - 2.44)	1.06 (0.65 - 1.94) ‡	0.94 (0.65 - 1.06)	1.94 (0.86 - 2.18)
IL-8 (pg/ml)	B	5.35 (3.84 - 7.96)	8.48 (6.54 - 9.62)	4.6 (3.74 - 6.34) †	6.34 (4.6 - 6.94)	5.24 (3.73 - 8.22)
IL-8 (pg/ml)	C1	5.6 (4.1 - 8)	7.43 (6.43 - 13.23)	4.56 (3.18 - 5.6)	5.09 (4.1 - 6.58)	5.79 (4.3 - 8.16)
IL-8 (pg/ml)	C2	6.32 (4.31 - 8.65)	8.61 (6.29 - 11.7)	5.35 (3.38 - 7.12)	6.47 (6.08 - 7.74)	6.26 (4.15 - 8.86)
TNF-α (pg/ml)	B	3.39 (2.79 - 4.28)	4.12 (3.37 - 4.72)	3.21 (2.55 - 3.6)	2.55 (2.47 - 3.39)	3.5 (3.2 - 4.33)
TNF-α (pg/ml)	C1	3.62 (2.45 - 4.79)	4.6 (3.77 - 5.69)	2.68 (2.07 - 4.02)	2.68 (2.35 - 4.41)	3.74 (2.82 - 4.84)
TNF-α (pg/ml)	C2	3.59 (2.74 - 4.8)	3.93 (3.31 - 5.11)	3.56 (2.46 - 4.25)	3.68 (3.28 - 4.05) ‡	3.58 (2.37 - 4.87)

Continuous variables are presented as median (interquartile range). Baseline values significantly different between initial combination versus monotherapy groups are marked by a *. Baseline values significantly different between CTD-PAH versus IPAH are marked by a †. ‡ notes a significant difference between the marked value and the baseline value for the addressed parameter and group. B, baseline; C1, first checkup; C2, second checkup; CTD-PAH, connective tissue disease pulmonary arterial hypertension; HPAH, hereditary pulmonary arterial hypertension; IPAH, idiopathic pulmonary arterial hypertension; FGF-2, fibroblast growth factor 2; IL, interleukin; IPAH, idiopathic pulmonary arterial hypertension; PIGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1; Tie-2, angiotensin II type 2 receptor; TNF-α, tumor necrosis factor α; VEGF, vascular endothelial growth factor.