

Supplemental Tabel 1: Endothelial Biomarkers

Endothelial Biomarkers					
	Placebo	Prostacyclin	Time	Group	Time*Group
Thrombomodulin (ng/ml)					
0 Hours	9.22 (7.83-10.48)	7.91 (7.13-12.19)			
6 Hours	8.30 (7.19-10.72)	7.52 (6.55-10.95)			
24 Hours	8.71 (7.08-11.33)	7.09 (6.22-9.67)			
48 Hours	8.57 (7.77-11.20)	6.91 (5.75-9.76)	0.0002	0.67	0.16
72 Hours	7.69 (5.83-9.98)	6.78 (5.43-9.80)			
96 Hours	7.56 (5.53-8.68)	7.11 (6.78-9.94)	0.0006	0.79	0.021
E-Selectin (ng/ml)					
0 Hours	95.81 (70.51-121.38)	109.89 (80.39-121.90)			
6 Hours	96.33 (70.01-126.24)	118.60 (89.59-132.67)			
24 Hours	124.27 (89.85-143.09)	125.41 (82.19-140.11)			
48 Hours	123.62 (95.04-146.51)	99.44 (82.43-123.73)	0.0002	0.50	0.10
72 Hours	109.37 (81.29-130.36)	107.37 (80.72-116.23)			
96 Hours	106.13 (57.69-120.30)	105.80 (79.67-131.10)	0.0001	0.78	0.27
VEcad (ng/ml)					
0 Hours	2122.70 (1950.70-2307.90)	2392.70 (1878.30-2710.90)			
6 Hours	2103.00 (1947.20-2759.80)	2498.50 (1904.20-2679.00)			
24 Hours	1963.20 (1860.00-2333.20)	2150.20 (1797.60-2483.90)			
48 Hours	1896.90 (1773.60-2372.50)	2005.60 (1709.70-2458.40)	<0.0001	0.53	0.81
72 Hours	1887.75 (1687.50-2334.20)	2223.80 (1580.40-2279.10)			
96 Hours	1933.75 (1614.70-2245.80)	2302.60 (1896.10-2553.00)	<0.0001	0.94	0.03
VEGF (ng/ml)					
0 Hours	0.58 (0.00-23.33)	18.56 (0.00-32.44)			
6 Hours	25.01 (5.84-49.02)	49.59 (16.58-77.43)			
24 Hours	35.46 (21.60-80.69)	46.11 (27.50-67.64)			
48 Hours	28.39 (14.22-50.49)	24.45 (15.10-33.85)	0.008	0.50	0.60
72 Hours	24.78 (14.88-37.94)	24.45 (13.43-36.24)			
96 Hours	23.38 (15.76-39.02)	24.33 (11.09-29.96)	0.17	0.61	0.89
Syndecan (ng/ml)					
0 Hours	102.62 (58.14-116.52)	79.95 (26.42-108.46)			
6 Hours	63.25 (37.97-88.65)	37.01 (21.52-73.30)			
24 Hours	39.75 (26.76-67.84)	24.80 (18.44-51.21)			
48 Hours	42.02 (29.78-64.47)	27.21 (17.03-46.70)	<0.0001	0.44	0.12
72 Hours	36.73 (25.00-57.28)	32.47 (25.62-109.04)			
96 Hours	39.92 (28.71-61.65)	42.14 (24.37-116.08)	<0.0001	0.56	0.004
Nucleosomes (%)					
0 Hours	13.90 (6.65-18.37)	9.07 (4.06-25.42)			
6 Hours	4.97 (3.29-7.74)	3.35 (2.17-5.94)			
24 Hours	4.64 (3.03-7.12)	2.55 (1.93-3.40)			
48 Hours	8.02 (4.50-10.46)	4.25 (2.36-5.25)	<0.0001	0.19	0.45
72 Hours	7.80 (3.90-9.64)	5.98 (4.86-13.41)			
96 Hours	6.24 (4.52-10.23)	8.25 (5.88-38.46)	<0.0001	0.88	0.0002
Adrenaline (pg/L)					
0 Hours	798.96 (258.92-1146.20)	335.87 (108.63-774.74)			
6 Hours	110.88 (49.55-297.80)	86.78 (33.00-210.52)			
24 Hours	38.64 (21.31-82.27)	32.41 (23.36-78.82)			
48 Hours	55.20 (33.73-165.93)	27.06 (15.71-239.31)	<0.0001	0.62	0.88
72 Hours	41.82 (15.20-88.58)	32.09 (21.30-182.31)			
96 Hours	55.29 (30.15-86.86)	29.34 (18.23-89.82)	<0.0001	0.57	0.42
Noradrenaline (pg/L)					
0 Hours	1572.21 (633.13-4802.59)	634.44 (487.54-4836.63)			
6 Hours	3452.74 (2476.91-9554.31)	2737.62 (1008.96-15450.34)			
24 Hours	4463.87 (2555.09-11345.82)	5172.42 (1319.41-11228.25)			
48 Hours	1608.65 (491.16-5137.72)	1159.00 (398.59-2706.68)	0.0002	0.30	0.89
72 Hours	1006.01 (622.12-2164.60)	313.00 (153.13-1222.22)			
96 Hours	646.07 (388.07-1222.85)	324.85 (116.47-499.12)	<0.0001	0.005	0.40
Data are presented as medians (IQR) or n (%). Patients stratified according to 4 treatment arms (Placebo/65mmHg; Placebo 65mmHg+10%; Prostacyclin/65mmHg; Prostacyclin/65mmHg + 10%) and were compared using baseline corrected Proc Mixed repeated measurement models 1) Group and Time and model 2) Group*Time at the 48 and 96-hour endpoints.					

Supplemental Table 2: Hemostasis

Hemostasis			
	Placebo	Prostacyclin	p
TEG Citrated Kaolin			
Reaction Time (minutes)	7.2 (5.9-8.1)	7.2 (6.2-8.8)	0.75
Angle (degrees)	69.1 (63.8-71.5)	69.45 (67.6-71.4)	0.77
Maximum Amplitude (MA)	68.6 (62.9-71.5)	70.45 (67.4-74.3)	0.20
G (d/sc)	10928.3 (8491-12540)	11924.95 (10333-14477)	0.22
Lysis 30%	0.3 (0-0.9)	0.5 (0.3-1)	0.29
TEG Functional Fibrinogen			
Reaction Time (minutes)	3.4 (2.9-4.35)	3.4 (2.9-4.2)	0.84
Angle (degrees)	54.4 (45.55-57.15)	52.6 (48.5-57.9)	0.92
Maximum Amplitude (MA)	27.6 (24.7-30.5)	27.85 (25.9-30.5)	0.78
G (dynes/cm ²)	1901 (1640-2191)	1932 (1748-2197)	0.74
Lysis 30%	0 (0-0)	0 (0-0)	1.00
Multiplate			
ADP (U)	54.15 (34.8-59.4)	48.4 (25.8-61.6)	0.65
ASPI (U)	64.2 (40.55-79.2)	58.4 (24-83.4)	0.60
TRAP (U)	109.3 (83-125.8)	106.3 (94.2-119.1)	1.00
RISTO (U)	66 (56.8-78.5)	63.85 (59.1-88)	0.91

Data are presented as medians (IQR) or n (%). Patients stratified according to Placebo/Prostacyclin at the 48-hour endpoint and compared using Mann Whitney U. R, reaction time; MA, maximum amplitude; Ly30 %, lysis after 30 minutes. ASPI, arachidonic acid; ADP, adenosin diphosphat; TRAP, thrombin-receptor activating peptide (TRAP)-6 ; RISTO, Ristocetin; U, area under the curve. p<0.05 significant; p >0.05 non-significant (NS)

Supplemental Table 3: Hemodynamics

Hemodynamics					
	Placebo	Prostacyclin	Time p	Group p	Time*Group p
Arterial blood pressure (mmHg)					
0 Hours	69.5 (62.5-79.5)	68 (62-77.5)			
6 Hours	68 (65-73)	69 (68-71)			
24 Hours	69.5 (64-76)	69 (65-76)			
48 Hours	72.5 (68.5-85.5)	74 (70-79)	0.03	0.91	0.65
72 Hours	81 (67-92)	79 (72-107)			
96 Hours	70 (66-90)	96 (93-102)	0.0002	0.81	0.46
Systolic Blood pressure					
0 Hours	102 (89.6-111.7)	96.8 (86-105.6)			
48 Hours	114.4 (101-129)	105 (97-130)	0.002	0.44	0.96
96 Hours	123.7 (114.2-141.7)	149 (142-160.6)	<0.0001	0.53	0.17
Diastolic Blood pressure					
0 Hours	57.8 (52.8-66)	56.1 (50-62)			
48 Hours	59 (57-69)	57.1 (50-63)	0.25	0.27	0.57
96 Hours	62.5 (54-71.3)	73 (66-94)	0.002	0.97	0.55
Puls					
0 Hours	76(61-89.5)	71(56.5-90)			
6 Hours	69(54-82)	70(57-82)			
24 Hours	69(58-81)	65(54-71)			
48 Hours	88(71-109)	74(65-104)	0.0002	0.80	0.14
72 Hours	86.5(74-95)	98.5(76.5-106)			
96 Hours	88(77-92)	70(60-97)	<0.0001	0.67	0.11
CentralTp (Celcius)					
0 Hours	36 (35.4-36.6)	35.5 (35.35-36.05)			
6 Hours	36.1 (36-36.1)	36.1 (35.9-36.2)			
24 Hours	36.1 (36-36.3)	36.2 (36.1-36.3)			
48 Hours	37.3 (37.1-37.85)	37.8 (37.35-38.65)	<0.0001	0.30	0.04
72 Hours	37.75 (37.4-38.2)	38.1 (37.75-38.6)			
96 Hours	37.85 (37.5-38.5)	37.45 (37.3-37.9)	<0.0001	0.11	0.09
Dopamine (µg/kg/24hours)					
24H	0 (0-2100)	0 (0-1932)			
48H	3300 (0-6840)	0 (0-1440)			
72H	120 (0-4053)	0 (0-0)			
96H	0 (0-0)	0 (0-0)	0.02	0.77	0.93
Noradrenaline (µg/kg/24hours)					
24H	85.74(42-189.6)	152.4(15.84-182.4)			
48H	187.07(81.6-300.48)	110.4(17.82-306.72)			
72H	65.46(1.56-226.2)	13.44(0-54.42)			
96H	0(0-73.8)	0(0-28.8)	0.004	0.04	0.88
Adrenaline (µg/kg/24hours)					
24H	0 (0-0)	0 (0-0)			
48H	0 (0-0)	0 (0-0)			
72H	0 (0-0)	0 (0-0)			
96H	0 (0-0)	0 (0-0)	*	*	*
Data are presented as medians (IQR) or n (%). Patients stratified according to 4 treatment arms (Placebo/65mmHg; Placebo 65mmHg+10%; Prostacyclin/65mmHg; Prostacyclin/65mmHg + 10%) and were compared using baseline corrected Proc Mixed repeated measurement models 1) Group and Time and model 2) for Group*Time at the 48 and 96-hour endpoints.					

Supplemental Tabel 4: Arterial Blood Gas Analysis

Arterial Blood Gas					
	Placebo	Prostacyclin	Time	Group	Time*Group
pH					
0 Hours	7.23 (7.21-7.31)	7.26 (7.17-7.3)			
6 Hours	7.32 (7.26-7.38)	7.34 (7.31-7.41)			
24 Hours	7.35 (7.3-7.37)	7.36 (7.33-7.37)			
48 Hours	7.37(7.37-7.41)	7.41 (7.36-7.41)	<0.0001	0.18	0.74
72 Hours	7.41 (7.38-7.44)	7.39 (7.37-7.44)			
96 Hours	7.45 (7.43-7.48)	7.45 (7.41-7.45)	<0.0001	0.75	0.42
PaO ₂ (mmHg)					
0 Hours	16.5 (11.8-24.6)	14.95 (11.35-32)			
6 Hours	13.8 (11.2-16.5)	13.4 (11.6-15.4)			
24 Hours	10.6 (9.59-12.4)	11.8 (10.9-12.8)			
48 Hours	11.95 (10.85-13.1)	11 (10.1-13)	<0.0001	0.66	0.46
72 Hours	11.6 (10.5-12.6)	11 (10.3-12.8)			
96 Hours	12.5 (10.3-13.6)	9.66 (8.97-12.5)	<0.0001	0.34	0.89
PaCO ₂ (mmHg)					
0 Hours	5.69 (5.18-6.28)	5.42 (4.905-6.27)			
6 Hours	4.99 (4.58-5.42)	4.635 (4.31-5.09)			
24 Hours	5.06 (4.69-5.43)	4.61 (4.38-5.05)			
48 Hours	4.97 (4.69-5.655)	4.56 (4.5-4.83)	0.004	0.03	0.83
72 Hours	5.07 (4.58-5.56)	5.4 (4.41-6.41)			
96 Hours	4.73 (4.365-5.215)	5.35 (5.33-5.5)	0.0003	0.84	0.66
FiO ₂					
0 Hours	57.5 (45-80)	60 (40-70)			
6 Hours	40 (30-65)	47.5 (40-55)			
24 Hours	35 (25-40)	40 (30-55)			
48 Hours	38 (29-45)	40 (32-45)	<0.0001	0.39	0.53
72 Hours	35 (30-40)	42 (33.5-55)			
96 Hours	37 (30.5-47.5)	36 (21-45)	<0.0001	0.09	0.32
Bicarbonate ion (mmol/L)					
0 Hours	17.8 (15.7-20)	18.4 (16.1-20.6)			
6 Hours	19.7 (18.2-22.2)	20.2 (19.4-21.6)			
24 Hours	20.8 (19.55-22.65)	20.4 (19.2-21.6)			
48 Hours	21.75 (20.65-23.55)	22.4 (20.3-23.5)	<0.0001	0.85	0.70
72 Hours	23.85 (22.9-25.8)	24.4 (20.1-26.8)			
96 Hours	26.3 (24.25-27.35)	28.1 (25.3-28.2)	<0.0001	0.86	0.18
Lactate (mmol/L)					
0 Hours	4.1 (2.2-8.5)	5.7 (3.5-8.4)			
6 Hours	1.3 (0.9-2.7)	1.05 (0.9-1.3)			
24 Hours	1.3 (0.8-1.85)	1.3 (1-1.7)			
48 Hours	1.2 (0.8-1.5)	1.4 (1-1.95)	<0.0001	0.87	0.14
72 Hours	0.9 (0.8-1.2)	1.3 (1-1.7)			
96 Hours	1 (0.85-1.25)	0.9 (0.9-1)	<0.0001	0.98	0.62
Saturation (%)					
0 Hours	96 (85.5-99)	95 (93-98)			
6 Hours	97.4 (96.1-98.2)	97.6 (96.1-98.3)			
24 Hours	95.7 (94-97.2)	96.9 (95.8-97.2)			
48 Hours	97 (95.55-97.3)	96.1 (94.3-97.5)	0.17	0.49	0.55
72 Hours	96.8 (95.6-97.7)	95.4 (95.3-97.7)			
96 Hours	97 (95.8-97.7)	95 (94.1-97.6)	<0.0001	0.96	0.73
Base Excess* (mmol/L)					
0 Hours	-7.1 (-10.2--4.6)	-6.35 (-9.9--4.4)			
6 Hours	-5.6 (-7.4--3.5)	-4.75 (-5.8--3.9)			
24 Hours	-4.4 (-6.25--1.7)	-5.6 (-6.9--3.4)			
48 Hours	-3.2 (-4.6--1.15)	-1.9 (-5--1.3)	0.002	0.94	0.21
72 Hours	-0.8 (-2.05-1.2)	0 (-6.4-3)			
96 Hours	1.85 (-0.55-3.2)	4.1 (2.2-4.3)	<0.0001	0.92	0.58

Data are presented as medians (IQR) or n (%). Patients stratified according to 4 treatment arms (Placebo/65mmHg; Placebo 65mmHg+10%; Prostacyclin/65mmHg; Prostacyclin/65mmHg + 10%) and were compared using baseline corrected Proc Mixed repeated measurement models 1) Group and Time and model 2) Group*Time at the 48 and 96-hour endpoints.

Supplemental Tabel 5: Conventional Coagulation Markers

Coagulation Markers					
	Placebo	Prostacyclin	Time	Group	Time*Group
Antithrombin (x10 ³ IE/L)					
0 Hours	0.81 (0.68-0.96)	0.81 (0.72-1.01)			
6 Hours	0.83 (0.72-0.95)	0.95 (0.85-0.97)			
24 Hours	0.76 (0.66-0.88)	0.82 (0.77-0.92)			
48 Hours	0.7 (0.62-0.86)	0.83 (0.75-0.92)	0.0002	0.64	0.74
72 Hours	0.71 (0.64-0.87)	0.94 (0.76-1.08)			
96 Hours	0.845 (0.7-0.96)	0.93 (0.8-0.99)	<0.0001	0.60	0.63
Activated partial thromboplastin time (APPT) (s)					
0 Hours	30 (25-90)	30 (25.5-34)			
6 Hours	30 (26-45)	30 (26-37)			
24 Hours	33 (27-35)	34 (30-36)			
48 Hours	32 (29-35)	31.5 (30-35)	0.34	0.66	0.31
72 Hours	31 (29-33)	31.5 (29-36)			
96 Hours	29 (28-34)	33 (31-34)	0.05	0.25	0.22
International Normalized Ratio (INR)					
0 Hours	1.2 (1.1-1.3)	1.1 (1-1.2)			
6 Hours	1.1 (1-1.2)	1 (1-1.1)			
24 Hours	1.2 (1.1-1.2)	1.2 (1.1-1.2)			
48 Hours	1.3 (1.2-1.3)	1.2 (1.1-1.2)	<0.0001	0.95	0.14
72 Hours	1.2 (1.1-1.2)	1.2 (1.1-1.2)			
96 Hours	1.1 (1.1-1.2)	1.1 (1-1.2)	0.0008	0.07	0.83
Fibrin D-dimer (mg FEU/l)					
0 Hours	9.25 (4.3-20.1)	5.6 (3.9-40.9)			
6 Hours	4 (1.7-6.1)	2.6 (1.8-14.5)			
24 Hours	1.4 (0.8-2.2)	1.1 (0.8-2.4)			
48 Hours	1.4 (1-2.4)	1 (0.9-1.5)	<0.0001	0.71	0.07
72 Hours	1.2 (0.9-2.2)	1.85 (1.3-4.7)			
96 Hours	1.7 (1.2-2.5)	2 (1.6-2.5)	<0.0001	0.11	0.01
Fibrinogen (μmol/L)					
0 Hours	7.95 (7.5-8.8)	9.3 (6.9-11.3)			
6 Hours	9.3 (7.8-10.7)	10.05 (8.5-11.1)			
24 Hours	12.4 (11.2-14.4)	13.9 (11.5-18.5)			
48 Hours	16.7 (15.3-19)	17.1 (15.2-19.3)	<0.0001	0.92	0.46
72 Hours	18.8 (16.3-22)	18.55 (16-19.8)			
Coagulation markers II. IV. (IE/L)					
0 Hours	0.74 (0.62-0.86)	0.77 (0.62-1.08)			
6 Hours	0.82 (0.67-0.95)	0.9 (0.78-1.04)			
24 Hours	0.75 (0.66-0.91)	0.75 (0.66-0.99)			
48 Hours	0.66 (0.55-0.72)	0.795 (0.65-0.82)	<0.0001	0.89	0.13
72 Hours	0.74 (0.63-0.87)	0.725 (0.67-0.81)			
96 Hours	0.815 (0.64-0.92)	0.82 (0.68-0.97)	0.39	0.37	0.70
Data are presented as medians (IQR) or n (%). Patients stratified according to 4 treatment arms (Placebo/65mmHg; Placebo 65mmHg+10%; Prostacyclin/65mmHg; Prostacyclin/65mmHg + 10%) and were compared using baseline corrected Proc Mixed repeated measurement models 1) Group and Time and model 2) Group*Time at the 48 and 96-hour endpoints.					

Supplemental Tabel 6: Organ Markers

Organ markers					
	Placebo	Prostacyclin	Time	Group	Time*Group
Liver markers					
Alanine aminotransferase (ALAT) (U/L)					
0 Hours	107 (73-175)	138 (54-441)			
6 Hours	102 (66-190)	115 (48-211)			
24 Hours	91 (58-128)	77 (41-140)			
48 Hours	79 (51-120)	62 (32-96)	<0.0001	0.98	0.10
72 Hours	61 (45-89)	59.5 (42-76)			
96 Hours	61 (46-79)	55 (50-63)	<0.0001	0.72	0.08
Albumin					
0 Hours	33 (31-36)	32 (30-35)			
6 Hours					
24 Hours	29 (26-31)	27 (25-29)			
48 Hours	26 (25-28)	25 (24-27)	<0.0001	0.75	0.32
72 Hours	24 (23-27)	27 (23-28)			
96 Hours	25 (22-29)	26 (23-28)	<0.0001	0.75	0.14
Basic Phosphatase (U/L)					
0 Hours	70 (62-97)	93 (67-107)			
6 Hours	60 (57-83)	77.5 (59-93)			
24 Hours	62 (49-72)	62 (52-79)			
48 Hours	63 (56-69)	63 (50-77)	<0.0001	0.90	0.21
72 Hours	64 (61-80)	69.5 (62-78)			
96 Hours	69 (63-86)	75 (62-81)	<0.0001	0.93	0.48
Bilirubin (µmol/L)					
0 Hours	7 (6-11)	5 (4-9)			
6 Hours	12 (9-17)	7 (5-16)			
24 Hours	13 (9-20)	7 (4-14)			
48 Hours	11 (9-16)	7 (5-13)	<0.0001	0.09	0.41
72 Hours	13 (9-15)	7 (5-8)			
96 Hours	11 (9-12)	8 (6-9)	<0.0001	0.16	0.47
Pancreatic marker					
Amylase (U/L)					
0 Hours	92 (68-125)	70 (58-113)			
6 Hours	79 (57-195)	56 (40-93)			
24 Hours	87 (47-204)	46 (41-56)			
48 Hours	67 (45-146)	41 (37-50)	0.051	0.66	0.16
72 Hours	65 (39-112)	55.5 (34-62)			
96 Hours	68.5 (43.5-116)	58 (43-71)	0.11	0.68	0.44
Kidney markers					
Glomerular filtration rate (eGFR) (ml/min)					
0 Hours	49 (42-65)	68 (41-71)			
6 Hours	54 (49-67)	60 (50-67)			
24 Hours	56.5 (38.5-73.5)	70 (33-80)			
48 Hours	56 (43-70)	34 (29-72)	0.70	0.37	0.17
72 Hours	67 (48-71)	56.5 (33-82)			
96 Hours	63 (48-83)	58 (56-80)	0.39	0.39	0.49
Phosphate (mmol/L)					
0 Hours	2.02 (1.42-2.53)	2.32 (1.7-2.57)			
6 Hours	1.18 (0.9-1.35)	1.2 (0.95-1.56)			
24 Hours	1.23 (0.91-1.41)	1.29 (0.97-1.42)			
48 Hours	0.96 (0.74-1.36)	0.92 (0.75-1.39)	<0.0001	0.74	0.81
72 Hours	0.72 (0.54-0.88)	0.855 (0.63-0.99)			
96 Hours	0.76 (0.62-0.88)	0.83 (0.72-0.88)	<0.0001	0.56	0.94
Carbamide (mmol/L)					
0 Hours	5.9 (4.9-7.3)	5.8 (4.9-7.2)			
6 Hours	7.25 (6.15-8.35)	7 (4.8-8.6)			
24 Hours	6.3 (4.7-8.5)	6.4 (3.7-10.7)			
48 Hours	5.7 (5-7.3)	5.9 (4-12.6)	<0.0001	0.69	0.46
72 Hours	5.9 (4.9-8.6)	7.85 (5.4-13.2)			
96 Hours	7 (5.6-10.1)	9.1 (5.2-11.1)	<0.0001	0.95	0.18
Creatinine (µmol/L)					
0 Hours	109 (101-133)	105 (94-139)			
6 Hours	118.5 (96-141.5)	97 (83-164)			
24 Hours	109 (90-139)	93 (74-169)			
48 Hours	102 (83-131)	92 (79-166)	0.88	0.85	0.57
72 Hours	94 (74-110)	91.5 (72-151)			
96 Hours	89 (70-110)	77 (70-91)	<0.0001	0.77	0.12
Cardiac markers					
TNT (ng/L)					
0 Hours	190 (113-467)	173 (111-306)			

4 Hours	1135 (580-3060)	1690 (255-3630)			
12 Hours	1205 (821-3120)	1330 (388-3050)			
24 Hours	1135 (443.5-2230)	1200 (389-2210)	<0.0001	0.98	0.99
CKMB (μmol/L)					
0 Hours	8 (5-26.4)	8.8 (6.95-17.45)			
4 Hours	57.95 (20.1-111)	59.5 (13.7-137)			
12 Hours	81.7 (32.1-159.5)	94.3 (20.7-227)			
24 Hours	67.1 (24.4-207)	64.5 (13.6-191)	<0.0001	0.82	0.56
CK (U/L)					
0 Hours	375(174-616)	212(140-398)			
4 Hours	1330(612-2480)	1430(335-1980)			
12 Hours	1890(848-2810)	1410(534-2780)			
24 Hours	1775(1110-3810)	1030(518-2870)	<0.0001	0.68	0.19
proBNP (pmol/L)					
0 Hours	53.4(19.3-130)	55.2(13.1-373)			
6 Hours	124(59.9-225)	202(68.1-237)			
24 Hours	203(102-361)	282(109-483)			
48 Hours	228(103-447)	296(123-514)	<0.0001	0.48	0.62
72 Hours	229(130-485)	392(136-896)			
96 Hours	265.5(126-522)	321(270-675)	0.0004	0.74	0.48
Cerebral markers					
S100 calcium-binding protein B (S100B) (μmol/L)					
24 Hours	0.105 (0.07-0.19)	0.08 (0.05-0.1)			
48 Hours	0.09 (0.06-0.12)	0.06 (0.05-0.11)			
72 Hours	0.05 (0.05-0.065)	(-)	0.75	0.23	*
Neuron specific enolase (NSE) (μg/L)					
24 Hours	28.4 (21.2-35.7)	28.25 (22.9-31.6)			
48 Hours	23.7 (19.3-42)	25.8 (18.5-36)			
72 Hours	33 (17-125)	13 (10-272)	0.74	0.78	0.91
Data are presented as medians (IQR) or n (%). Patients stratified according to 4 treatment arms (Placebo/65mmHg; Placebo 65mmHg+10%; Prostacyclin/65mmHg; Prostacyclin/65mmHg + 10%) and were compared using baseline corrected Proc Mixed repeated measurement models 1) Group and Time and model 2) Group*Time at the 48 and 96-hour endpoints.					

Supplemental Tabel 7: Electrolytes

Electrolytes					
	Placebo	Prostacyclin	Time	Group	Time*Group
Calcium (mmol/L)					
0 Hours	1.145 (1.085-1.21)	1.18 (1.15-1.27)			
6 Hours	1.14 (1.09-1.19)	1.145 (1.11-1.17)			
24 Hours	1.13 (1.08-1.17)	1.17 (1.12-1.19)			
48 Hours	1.145 (1.09-1.18)	1.18 (1.13-1.19)	0.35	0.59	0.64
72 Hours	1.16 (1.12-1.19)	1.15 (1.1-1.16)			
96 Hours	1.175 (1.12-1.19)	1.2 (1.19-1.21)	0.20	0.45	0.36
Kalium (mmol/L)					
0 Hours	3.8 (3.55-4.15)	4 (3.8-4.3)			
6 Hours	4 (3.8-4.5)	4 (3.7-4.3)			
24 Hours	4.35 (4-4.6)	4 (3.8-4.4)			
48 Hours	4.2 (3.95-4.3)	4.1 (3.9-4.2)	0.10	0.006	0.47
72 Hours	4.1 (3.8-4.2)	3.9 (3.7-4.3)			
96 Hours	3.95 (3.8-4.2)	4 (3.7-4.1)	<0.0001	0.37	0.51
Magnesium (mmol/L)					
0 Hours	0.9 (0.83-1.08)	0.91 (0.85-1)			
6 Hours	0.87 (0.76-1.06)	0.8 (0.75-0.88)			
24 Hours	0.8 (0.73-0.93)	0.78 (0.67-0.82)			
48 Hours	0.79 (0.75-0.85)	0.79 (0.71-0.97)	0.003	0.96	0.31
72 Hours	0.81 (0.75-0.85)	0.835 (0.77-0.9)			
96 Hours	0.82 (0.77-0.86)	0.91 (0.78-1.04)	0.002	0.94	0.37
Natrium (mmol/L)					
0 Hours	139 (136-140)	139 (138-140)			
6 Hours	140 (138-142)	139.5 (138-142)			
24 Hours	141 (139-143)	142 (140-145)			
48 Hours	141 (139-143)	145 (140-146)	0.001	0.86	0.03
72 Hours	142 (140-144)	145.5 (144-148)			
96 Hours	144 (141-146)	147 (144-148)	<0.0001	0.95	0.41
Other					
Pro-Calcitonin (µg/L)					
0 Hours	0.1(0.09-0.18)	0.11(0.07-0.16)			
6 Hours	1.2(0.33-4.01)	0.45(0.29-3.27)			
24 Hours	1.84(0.4-8.77)	1.07(0.31-3.98)			
48 Hours	1.305(0.355-6.105)	0.62(0.22-1.73)	<0.0001	0.41	0.38
72 Hours	0.535(0.265-2.115)	0.45(0.18-1.1)			
96 Hours	0.38(0.2-0.95)	0.235(0.125-0.7)	<0.0001	0.46	0.64
Glucose (mmol/L)					
0 Hours	11.2 (8.6-12.8)	10.15 (6.05-14.05)			
6 Hours	8.4 (7-11.4)	7.6 (6.9-8.7)			
24 Hours	7.35 (6.8-8.55)	7.6 (6.9-8.5)			
48 Hours	7.5 (6.5-9.45)	7.7 (6.9-8.2)	<0.0001	0.77	0.26
72 Hours	7.8 (6.9-9.3)	7.2 (6.9-9)			
96 Hours	8.3 (6.55-9.25)	8.5 (7.2-8.6)	<0.0001	0.91	0.92
C- Reactive protein (mg/L)					
0 Hours	2 (1-2)	3.5 (1.5-5)			
6 Hours	8 (4.5-14)	10 (4-13)			
24 Hours	106 (67-128)	109 (52-185)			
48 Hours	212 (147-259)	128 (104-248)	<0.0001	0.10	0.07
72 Hours	147 (103-223)	104 (63-179)			
96 Hours	84.5 (60-145)	71 (54-75)	<0.0001	0.27	0.12
Data are presented as medians (IQR) or n (%). Patients stratified according to 4 treatment arms (Placebo/65mmHg; Placebo 65mmHg+10%; Prostacyclin/65mmHg; Prostacyclin/65mmHg + 10%) and were compared using baseline corrected Proc Mixed repeated measurement models 1) Group and Time and model 2) Group*Time at the 48 and 96-hour endpoints.					

Supplemental Tabel 8: Hematology

Hematology					
	Placebo	Prostacyclin	Time	Group	Time*Group
Hemoglobin (mmol/L)					
0 Hours	9 (8-9.4)	8.35 (8-8.8)			
6 Hours	8.9 (8.2-9.7)	8.65 (8-9.4)			
24 Hours	8.5 (7.5-9.1)	8.3 (7.7-8.8)			
48 Hours	7.6 (6.55-8.25)	7.4 (7.2-7.6)	<0.0001	0.98	0.86
72 Hours	7.2 (6.2-7.5)	6.7 (6.6-7.5)			
96 Hours	6.8 (5.75-7.3)	6.7 (6.7-6.9)	<0.0001	0.70	0.88
Myoglobin (µg/L)					
0 Hours	928 (544-2770)	1200 (570-2070)			
6 Hours	1350 (629-2230)	963 (222-1580)			
24 Hours	573 (210-1240)	343 (127-878)			
48 Hours	238 (169-556)	215 (96-405)	0.0001	0.31	0.97
72 Hours	196 (115-447)	122.5 (86-516)			
96 Hours	140 (109-199)	93 (68-315)	<0.0001	0.88	0.10
Leukocytes (× 10 ⁹ /L)					
0 Hours	14.9 (13-20.8)	16.7 (15.1-19.1)			
6 Hours	15.05 (11.55-20.6)	16.3 (13.9-19)			
24 Hours	13 (11.7-16.1)	12.4 (9.4-17.6)			
48 Hours	12.8 (10.3-16.6)	11 (8.4-15.2)	0.01	0.89	0.35
72 Hours	10.2 (8.9-13.1)	9.65 (7.8-11.4)			
96 Hours	9.2 (7.3-12.2)	8.8 (6.4-9.4)	<0.0001	0.97	0.85
Neutrophilocytes (× 10 ⁹ /L)					
0 Hours	10.7 (7.8-16.7)	13 (10.8-14.4)			
6 Hours	13.5 (8.6-17.2)	14.8 (11.3-18.1)			
24 Hours	10.7 (8.5-13.25)	9.2 (6.9-14.2)			
48 Hours	10.35 (8.35-15.1)	8.5 (6.5-13.6)	0.0075	0.81	0.14
72 Hours	8.25 (6.9-10.6)	7.85 (6-9.4)			
96 Hours	7 (5.5-9.5)	6.7 (5-7.4)	0.0006	0.17	0.34
Lymphocytes (× 10 ⁹ /L)					
0 Hours	2.5(1.4-3.9)	2.1(1.2-4.4)			
6 Hours	1.3(0.9-1.7)	1.4(0.7-1.9)			
24 Hours	1.35(1-1.9)	1(0.8-1.8)			
48 Hours	0.85(0.65-1.15)	0.8(0.6-1.6)	0.001	0.97	0.82
72 Hours	0.85(0.7-1.4)	1.05(0.7-1.4)			
96 Hours	1.05(0.8-1.6)	0.8(0.8-1.3)	0.005	0.15	0.27
Eosinophilocytes (× 10 ⁹ /L)					
0 Hours	0.11 (0.03-0.21)	0.14 (0.06-0.29)			
6 Hours	0.01 (0-0.03)	0.01 (0.01-0.08)			
24 Hours	0.08 (0-0.215)	0.09 (0.01-0.23)			
48 Hours	0.01 (0-0.085)	0.01 (0-0.05)	<0.0001	0.29	0.64
72 Hours	0.065 (0-0.16)	0.015 (0.01-0.07)			
96 Hours	0.09 (0.02-0.25)	0.06 (0.03-0.1)	<0.0001	0.36	0.96
Basophilocytes (× 10 ⁹ /L)					
0 Hours	0.06 (0.04-0.09)	0.07 (0.04-0.11)			
6 Hours	0.04 (0.03-0.06)	0.04 (0.03-0.06)			
24 Hours	0.05 (0.03-0.07)	0.05 (0.03-0.06)			
48 Hours	0.03 (0.02-0.04)	0.03 (0.02-0.05)	<0.0001	0.93	0.39
72 Hours	0.02 (0.01-0.04)	0.025 (0.02-0.03)			
96 Hours	0.03 (0.02-0.05)	0.02 (0.02-0.03)	<0.0001	0.88	0.79
Monocytes (× 10 ⁹ /L)					
0 Hours	0.6 (0.4-0.9)	0.7 (0.5-0.9)			
6 Hours	1.4 (0.8-1.8)	1 (0.9-1.3)			
24 Hours	1 (0.8-1.3)	0.9 (0.7-1.2)			
48 Hours	0.8 (0.65-1.15)	0.9 (0.7-1)	0.0008	0.98	0.89
72 Hours	0.65 (0.5-1)	0.8 (0.6-1)			
96 Hours	0.8 (0.7-0.9)	0.8 (0.5-1.1)	<0.0001	0.35	0.97
Platelets (× 10 ⁹ /L)					
0 Hours	231 (194-282)	265 (246-282)			
6 Hours	248 (205-290)	265 (249-283)			
24 Hours	202 (173-253)	228 (187-235)			
48 Hours	179 (143-199)	194 (174-216)	<0.0001	0.91	0.50
72 Hours	167.5 (145-206)	169.5 (144-173)			
96 Hours	192 (156-244)	182 (160-200)	<0.0001	0.99	0.31
Data are presented as medians (IQR) or n (%). Patients stratified according to 4 treatment arms (Placebo/65mmHg; Placebo 65mmHg+10%; Prostacyclin/65mmHg; Prostacyclin/65mmHg + 10%) and were compared using baseline corrected Proc Mixed repeated measurement models 1) Group and Time and model 2) Group*Time at the 48 and 96-hour endpoints.					