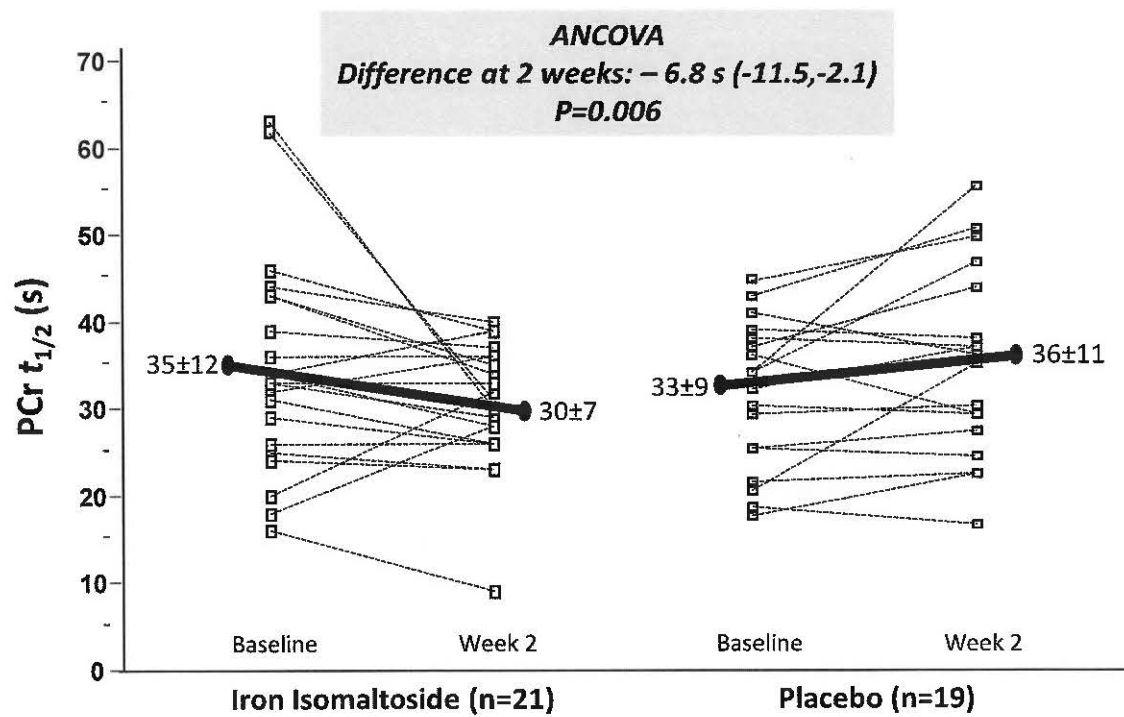


**APPENDIX 6: ENDPOINTS FOR TOTAL POPULATION**

	Placebo (n=19)	Iron Isomaltoside (n=21)	Difference (95% CI)	ANCOVA P-value
<b>Primary endpoint</b>				
PCr t <sub>1/2</sub> , s	36±11	30±7	-6.8(-11.5,-2.1)	<b>0.006</b>
<b>Secondary endpoints</b>				
ADP t <sub>1/2</sub> , s	24±9	20±6	-5.3(-9.7,-0.9)	<b>0.02</b>
Hemoglobin, g/L	127±14	130±13	2.4(-3.5,8.4)	0.41
Ferritin, ng/mL	57(41-84)	369(232-495)	304(217,391)	<b>&lt;0.0001</b>
Transferrin saturation, %	21±9	29±6	6.8(2.7,10.8)	<b>0.002</b>
NYHA class	2.6±0.5	2.3±0.5	-0.23(-0.46,-0.01)	<b>0.04</b>
6 min walking distance, m	324±67	347±72	15(-10,40)	0.24
Pre-exercise Borg dyspnea score	8±2	7±1	-0.6(-1.5,0.2)	0.12
Post-exercise Borg dyspnea score	15±2	12±3	-2.0(-3.7,-0.3)	<b>0.02</b>
Peak VO <sub>2</sub> /kg, mL/kg/min	14.9±3.5	16.8±4.7	0.5(-1.0,1.9)	0.54
KCCQ overall score	55±24	68±17	12.7(-7.7,33.2)	0.18
LV ejection fraction, %	39±8	41±7	2.2(-1.1,5.6)	0.19
NT-proBNP, pg/mL	334(180-827)	1623(281-2453)	289(-461,1040)	0.44
Resting PCr, mM	40±5	40±6	-0.2(-3.5,3.0)	0.89
Exercise PCr, mM	26±6	25±6	-0.3(-3.6,3.0)	0.86
Resting Pi, mM	3.8±1.1	4.0±1.0	0.3(-0.3,0.8)	0.33
Exercise Pi, mM	18.2±7.2	17.6±6.7	-0.9(-5.0,3.2)	0.66
Resting pH	7.01±0.3	7.01±0.3	-0.01(-0.02,0.01)	0.44
Exercise pH	6.99±0.06	6.97±0.07	0(-0.04,0.04)	0.97
Resting ADP, μM	7±5	8±5	0.9(-2.0,3.8)	0.52
Exercise ADP, μM	34±15	37±18	1.2(-8.1,10.5)	0.80
<b>Safety endpoints</b>				
Systolic blood pressure, mm Hg	119±14	127±12	7.1(-0.3,14.5)	0.06
Diastolic blood pressure, mm Hg	72±13	74±10	0.7(-5.5,6.8)	0.83
Heart rate, beats/min	74±12	71±10	-2.9(-8.8,3.1)	0.34
Respiratory rate, breaths/min	16±1	15±1	-0.7(-1.2,-0.2)	<b>0.009</b>
Creatinine, μmol/L	103±38	106±41	-3(-26,20)	0.80
Aspartate transaminase, IU/L	22±6	30±26	8(-4,21)	0.21
C-reactive protein, mg/L	4(2-8)	6(2-11)	0.4(-3.0,3.9)	0.79

**APPENDIX 7: INDIVIDUAL CHANGES IN PRIMARY ENDPOINT (PCr  $t_{1/2}$ )**



**APPENDIX 8: ANAEMIC AND NON-ANAEMIC SUBGROUP ANALYSES**

	Placebo	Iron Isomaltoside	Difference (95% CI)	ANCOVA P-value
<b>Anaemic patients</b>	<i>n</i> =9	<i>n</i> =11		
PCr $t_{1/2}$ , s	38±12	30±9	-8.4(-16.7,-0.2)	<b>0.04</b>
ADP $t_{1/2}$ , s	24±9	18±7	-6.3(-13.5,0.9)	0.08
Hemoglobin, g/dL	117±12	124±6	5.5(-2.7,13.8)	0.18
Ferritin, ng/mL	45±25	456±161	413(295,530)	<b>&lt;0.0001</b>
NYHA class	2.7±0.5	2.5±0.5	-0.3(-0.6,0.1)	0.09
<b>Non-anaemic patients</b>	<i>n</i> =10	<i>n</i> =10		
PCr $t_{1/2}$ , s	35±11	31±5	-5.2(-10.6,0.2)	0.06
ADP $t_{1/2}$ , s	24±9	21±5	-4.4(-9.6,0.9)	0.10
Hemoglobin, g/dL	135±9	137±15	0.5(-8.3,9.3)	0.72
Ferritin, ng/mL	67±24	274±149	176(68,284)	<b>0.003</b>
NYHA class	2.6±0.5	2.2±0.4	-0.2(-0.6,0.1)	0.23