

Online supplementary table 2. Study event table

Protocol activities	Screening period	Double-blind crossover part Visits/each treatment period			Open-label Follow-up extension				Post-treatment period
	Screening visit	Baseline Day 1 pre-dose	Day 5 ± 2	Day 14 ± 2	TC Week 2	Month 1	Month 3	Month 6	End-of-study visit
IC	x								
Demography and substance use	x								
Physical examination	x	x		x					x
Weight	x	x	x	x					x
Height and BMI	x								
Daytime oxygen saturation (SpO ₂)	x								
HR and BP	x	x	x	x		x	x	x	x
12-lead ECG	x	x ¹	x	x		x	x	x	x
Laboratory safety assessments									
Haematology	x	x		x		x	x	x	x
Chemistry	x	x ²		x ²		x ²	x ²	x ²	x ²
Urinalysis	x	x		x		x	x	x	x
Serology	x								
Testing ability to swallow capsules	x								
Pregnancy test for females of childbearing potential	x	x					x		x
24-hour Holter ECG	x			x					
Eligibility criteria and decision of entry	x								
Study treatment		x							
SVC	x ³	x ⁴	x ⁴	x ⁴		x ⁴	x ⁴	x ⁴	

SNP		x	x	x		x	x	x	
Overnight oxygen saturation (SpO2)		x	x	x		x	x	x	
Maximal grip strength and submaximal grip strength endurance		x	x	x					
CGI-C			x	x					
VAS addressing fatigue		x	x	x					
EQ-5D-5L		x		x		x	x	x	
ALSFRS-R scoring		x		x		x	x	x	
SF-36		x		x		x	x	x	
Blood sampling for levosimendan PK		x ⁵	x	x					
Blood sampling for riluzole concentration		x		x					
Blood sample for exploratory biomarkers		x				x		x	
Blood sample for PG		x ⁶							
Non-invasive ventilator support, permanent continuous ventilator dependence, tracheostomy and survival status		x							
Medical history and current medical conditions		x							
AEs and SAEs		x							
Concomitant treatments		x							

TC = telephone contact; BMI = body mass index; CGI-C = Clinical Global Impression of Change; VAS = visual analogue scale; EQ-5D-5L = European Quality of Life Five Dimension Five Level Scale; SF-36 = Short-form health survey; PK = pharmacokinetics; PG = pharmacogenomics; SAE =

¹ 3 baseline recordings

² Except thyroid-stimulating hormone (TSH)

³ Only in sitting position

⁴ In sitting and supine position

⁵ No pre-dose sample during the 1st treatment period

⁶ One sample preferably during visit 1 of the 1st treatment period